Access DB# 51157

SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: BAO QUN LI Examiner #: 78206 Date: 09/18/01
Art Unit: 1648 Phone Number 305-1695 Serial Number: 09/551,977
Mail Box and Bldg/Room Location: 8E 12 (5011) or 8B09 Results Format Preferred (circle) PAPER DISK E-MAIL

If more than one search is submitted, please prioritize searches in order of need.

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Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Compositions and methods for generating and immune response utilizing alphavirus-Basal Vector System

Inventors (please provide full names): John M. Polo, David A. Driver, Thomas Dubensky, Ilya Frolov, Jason Gardner

Earliest Priority Filing Date: April 14, 1999

***For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.**

Please search claims 17-23 directed to an alphavirus particle that infect dendritic cells (DC) where the DC include both human DC or non-human DC

Thanks

Point of Contact:
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Technical Info. Specialist
CM1 12C14 Tel: 306-4994

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STAFF USE ONLY	Type of Search	Vendors and cost where applicable
Searcher: Beverly 4994	NA Sequence (#)	STN ✓
Searcher Phone #:	AA Sequence (#)	Dialog
Searcher Location:	Structure (#)	Questel/Orbit
Date Searcher Picked Up:	Bibliographic	Dr.Link
Date Completed: 09-19-01	Litigation	Lexis/Nexis
Searcher Prep & Review Time: 12	Fulltext	Sequence Systems
Clerical Prep Time:	Patent Family	WWW/Internet
Online Time: 17	Other	Other (specify)

PTO-1590 (1-2000)

FILE 'CAPLUS' ENTERED AT 11:34:09 ON 19 SEP 2001
L1 3621 SEA FILE=CAPLUS ABB=ON PLU=ON ALPHAVIRUS OR ALPHA VIRUS OR VR2526 OR VR 2526 OR SINDBIS OR SEMLIKI FOREST OR ROSS RIVER OR VENEZUEL? EQUINE(1W)VIRUS
L6 37 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND (DENDRIT? OR DC(S)DENDRIT?)

L6 ANSWER 1 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:647459 CAPLUS
TITLE: Abundant GFP expression and LTP in hippocampal acute slices by in vivo injection of **sindbis** virus
AUTHOR(S): D'Apuzzo, Massimo; Mandolesi, Georgia; Reis, Gerald; Schuman, Erin M.
CORPORATE SOURCE: California Institute of Technology, Pasadena, CA, 91125, USA
SOURCE: J. Neurophysiol. (2001), 86(2), 1037-1042
CODEN: JONEA4; ISSN: 0022-3077
PUBLISHER: American Physiological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Virus-mediated gene transfer into neurons is a powerful tool for the anal. of neuronal structure and function. Recombinant **sindbis** virus has been previously used to study protein function in hippocampal neuron cultures as well as in hippocampal organotypic slice cultures. Nevertheless, some concern still exists about the physiol. relevance of these cultured prepns. Acute hippocampal slices are a widely used prepn. for the study of synaptic transmission, but currently recombinant gene delivery is usually achieved only through time-consuming transgenic techniques. In this study, we show that a subregion of the CA1 area in acute hippocampal slices can be specifically altered to express a gene of interest. A **sindbis** virus vector carrying an enhanced green fluorescent protein (EGFP) reporter was injected in vivo into the hippocampus of adult rats. After 18 h, rats were killed, and acute hippocampal slices, infected in the CA1 field, were analyzed morphol. and electrophysiol. Infected slices showed healthy and stable electrophysiol. responses as well as long-term potentiation. In addn., infected pyramidal cells were readily recognized in living slices by two-photon imaging. Specifically, the introduction of an EGFP-Actin fusion protein greatly enhanced the detection of fine processes and **dendritic** spines. We propose this technique as an efficient tool for studying gene function in adult hippocampal neurons.

L6 ANSWER 2 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:636194 CAPLUS
TITLE: Hybrid cell vaccines derived by fusion of an

allogeneic **dendritic** cells and a non-**dendritic** cells and uses in tumor and infection therapy

INVENTOR(S): Kanz, Lothar; Walden, Peter; Stuhler, Gernot
PATENT ASSIGNEE(S): Eberhard-Karls-Universitaet Tuebingen
Universitaetsklinikum, Germany

SOURCE: PCT Int. Appl., 42 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001062902	A1	20010830	WO 2000-EP2433	20000320
W: AE, AG, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, MA, MD, MG, MN, MW, MX, NO, NZ, PL, RU, SD, SG, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1130088	A1	20010905	EP 2000-105829	20000320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: DE 2000-10009030 A 20000227
US 2000-185334 P 20000228

AB The present invention relates to methods and compns. for treating and preventing cancer and infectious disease using hybrid cells formed by fusion of allogeneic **dendritic** cells and autologous non-**dendritic** cells which shares at least one class I MHC (major histocompatibility complex) allele. Such hybrid cells combine the vigorous alloreactivity of mature **dendritic** cells with the specific antigenicity of autologous tumor cells, thereby eliciting a highly specific and vigorous cytotoxic T lymphocytes (CTL) response. The invention also provides the methods for making hybrid cell vaccines and evaluating its cytotoxicity. For rapid and large-scale generation of hybrids, electrofusion is established as a two-step procedure: in the first step, tumor cells and **dendritic** cells (**DCs**) were dielectrophoretically aligned to from cell-cell conjugates; in the second step, a fusion pulse was applied, yielding 10-15% hybrid cell formation. The invention demonstrates that vaccine with tumor cell-**dendritic** cell hybrid results in regression of human metastatic renal cell carcinoma.

REFERENCE COUNT: 6
REFERENCE(S): (1) Celluzzi, C; JOURNAL OF IMMUNOLOGY 1998,

V160(7), P3081 CAPLUS
(2) Dana Farber Cancer Inst Inc; WO 9846785 A 1998 CAPLUS
(3) Guo, Y; SCIENCE 1994, V263(5146), P518 CAPLUS
(4) Kugler, A; BRITISH JOURNAL OF UROLOGY 1998, V82(4), P487 MEDLINE
(6) Kugler, A; NATURE MEDICINE 2000, V6(3), P332 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:563197 CAPLUS
TITLE: Changes in calcium currents and GABAergic spontaneous activity in cultured rat hippocampal neurons after a neurotropic influenza A virus infection
AUTHOR(S): Brask, J.; Owe-Larsson, B.; Hill, R. H.; Kristensson, K.
CORPORATE SOURCE: Department of Neuroscience, Karolinska Institutet, Stockholm, Swed.
SOURCE: Brain Res. Bull. (2001), 55(3), 421-429
CODEN: BRBUDU; ISSN: 0361-9230
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In order to study mechanisms by which a neurotropic strain of influenza A virus (A/WSN/33) may affect neuronal function or cause nerve cell death, hippocampal cultures from embryonic rats were infected with this virus. Approx. 70% of the neurons in the infected cultures became immunopos. for viral antigens and showed reduced voltage-dependent Ca2+ currents in whole-cell patch clamp recordings, but no changes in other membrane properties or in cytosolic Ca2+ concn. were seen. These immunopos. neurons underwent apoptosis 3-4 days after infection. Ca2+ channel inhibitors had no significant effect on neuronal survival. The immunoneg. population of neurons survived, but displayed increased frequency of miniature inhibitory postsynaptic currents of .gamma.-amino-butyric acid origin compared with controls. The frequency of .alpha.-amino-hydroxy-5-methylisoxazole-4-propionic acid hydrobromide (AMPA) receptor-mediated miniature excitatory postsynaptic currents was not altered. Viral nucleoproteins, overexpressed using the **Semliki Forest** virus system, were localized to the **dendritic** spines as shown by double immunolabeling with actinin, but did not by themselves cause neuronal death or changes in synaptic transmission as measured by AMPA-mediated excitatory postsynaptic currents. Our results show that an influenza A virus infection can cause selective

neurophysiol. changes in hippocampal neurons and that these can persist even after the viral antigens have been cleared.

L6 ANSWER 4 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:545880 CAPLUS
DOCUMENT NUMBER: 135:103358
TITLE: Novel non-lab. virus strains with improved oncolytic and/or gene delivery capabilities as compared to lab. virus strains, and uses thereof
INVENTOR(S): Coffin, Robert Stuart
PATENT ASSIGNEE(S): Biovex Limited, UK
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001053506	A2	20010726	WO 2001-GB229	20010122

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:		
GB 2000-1475	A	20000121
GB 2000-2854	A	20000208
GB 2001-288	A	20010105
GB 2001-430	A	20010106

AB The invention provides novel non-lab. virus strains, esp. herpes viruses such as HSV, with improved oncolytic and/or gene delivery capabilities as compared to lab. virus strains. The inventors have shown that two clin. isolates of HSV1 (strains JS1 and BL1) have enhanced replication in some human tumor cell lines as compared to the lab. HSV1 strain 17+. Although the invention is exemplified using HSV, it is equally applicable for other viruses, such as adenovirus, picornavirus, retrovirus, or **alphavirus**. In the provided virus strains, the gene encoding ICP34.5 was deleted, and this resulted in enhanced growth in tumor cells as compared to a similarly engineered lab. strain. The viruses also are engineered to express human GM-CSF or some other immunomodulatory protein. The

invention also provides methods and compns. for the treatment of cancer.

L6 ANSWER 5 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:354947 CAPLUS
DOCUMENT NUMBER: 135:120926
TITLE: Enhancement of **Sindbis** virus self-replicating RNA vaccine potency by linkage of Mycobacterium tuberculosis heat shock protein 70 gene to an antigen gene
AUTHOR(S): Cheng, Wen-Fang; Hung, Chien-Fu; Chai, Chee-Yin; Hsu, Keng-Fu; He, Liangmai; Rice, Charles M.; Ling, Morris; Wu, T.-C.
CORPORATE SOURCE: Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, MD, 21205, USA
SOURCE: J. Immunol. (2001), 166(10), 6218-6226
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Recently, self-replicating RNA vaccines (RNA replicons) have emerged as an effective strategy for nucleic acid vaccine development. Unlike naked DNA vaccines, RNA replicons eventually cause lysis of transfected cells and therefore do not raise the concern of integration into the host genome. We evaluated the effect of linking human papillomavirus type 16 E7 as a model Ag to Mycobacterium tuberculosis heat shock protein 70 (HSP70) on the potency of Ag-specific immunity generated by a **Sindbis** virus self-replicating RNA vector, SINrep5. Our results indicated that this RNA replicon vaccine contg. an E7/HSP70 fusion gene generated significantly higher E7-specific T cell-mediated immune responses in vaccinated mice than did vaccines contg. the wild-type E7 gene. Furthermore, our in vitro studies demonstrated that E7 Ag from E7/HSP70 RNA replicon-transfected cells can be processed by bone marrow-derived **dendritic** cells and presented more efficiently through the MHC class I pathway than can wild-type E7 RNA replicon-transfected cells. More importantly, the fusion of HSP70 to E7 converted a less effective vaccine into one with significant potency against E7-expressing tumors. This antitumor effect was dependent on NK cells and CD8+ T cells. These results indicated that fusion of HSP70 to an Ag gene may greatly enhance the potency of self-replicating RNA vaccines.
REFERENCE COUNT: 41
REFERENCE(S):
(1) Albert, M; J Exp Med 1998, V188, P1359 CAPLUS
(2) Albert, M; Nature 1998, V392, P86 CAPLUS
(4) Anthony, L; Vaccine 1999, V17, P373 CAPLUS
(5) Basu, S; Int Immunol 2000, V12, P1539 CAPLUS

(6) Berglund, P; AIDS Res Hum Retrovir 1997, V13, P1487 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 6 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:205129 CAPLUS
DOCUMENT NUMBER: 134:365427
TITLE: Infection of human **dendritic** cells by a **sindbis** virus replicon vector is determined by a single amino acid substitution in the E2 glycoprotein
AUTHOR(S): Gardner, Jason P.; Frolov, Ilya; Perri, Silvia; Ji, Yaying; MacKichan, Mary Lee; zur Megede, Jan; Chen, Minchao; Belli, Barbara A.; Driver, David A.; Sherrill, Scott; Greer, Catherine E.; Otten, Gillis R.; Barnett, Susan W.; Liu, Margaret A.; Dubensky, Thomas W.; Polo, John M.
CORPORATE SOURCE: Vaccines & Gene Therapy, Chiron Corporation, Emeryville, CA, 94608, USA
SOURCE: J. Virol. (2000), 74(24), 11849-11857
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability to target antigen-presenting cells with vectors encoding desired antigens holds the promise of potent prophylactic and therapeutic vaccines for infectious diseases and cancer. Toward this goal, we derived variants of the prototype **alphavirus** , **Sindbis** virus (SIN), with differential abilities to infect human **dendritic** cells. Cloning and sequencing of the SIN variant genomes revealed that the genetic determinant for human **dendritic** cell (**DC**) tropism mapped to a single amino acid substitution at residue 160 of the envelope glycoprotein E2. Packaging of SIN replicon vectors with the E2 glycoprotein from a DC-tropic variant conferred a similar ability to efficiently infect immature human DC, whereupon those DC were obsd. to undergo rapid activation and maturation. The SIN replicon particles infected skin-resident mouse DC in vivo, which subsequently migrated to the draining lymph nodes and upregulated cell surface expression of major histocompatibility complex and costimulatory mols. Furthermore, SIN replicon particles encoding human immunodeficiency virus type 1 p55Gag elicited robust Gag-specific T-cell responses in vitro and in vivo, demonstrating that infected DC maintained their ability to process and present replicon-encoded antigen. Interestingly, human and mouse DC were differentially infected by selected SIN variants, suggesting differences in receptor expression between human and murine DC. These data illustrate the tremendous potential of using a directed

approach in generating **alphavirus** vaccine vectors that target and activate antigen-presenting cells, resulting in robust antigen-specific immune responses.

REFERENCE COUNT: 50

REFERENCE(S):
(1) Akbari, O; J Exp Med 1999, V189, P169 CAPLUS
(2) Albert, M; Nature 1998, V392, P86 CAPLUS
(3) Banchereau, J; Nature 1998, V392, P245 CAPLUS
(4) Bender, A; J Immunol Methods 1996, V196, P121 CAPLUS
(5) Bhardwaj, N; J Exp Med 1997, V186, P795 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 7 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:196378 CAPLUS

TITLE: Enhancement of antitumor immune response in glioma models in mice by genetically modified **dendritic** cells pulsed with **Semliki Forest** virus-mediated complementary DNA

AUTHOR(S): Yamanaka, Ryuya; Zullo, Susan A.; Tanaka, Ryuichi; Blaese, Michael; Xanthopoulos, Kleanthis G.

CORPORATE SOURCE: Clinical Gene Therapy Branch, National Institutes of Health, Bethesda, MD, USA

SOURCE: J. Neurosurg. (2001), 94(3), 474-481
CODEN: JONSAC; ISSN: 0022-3085

PUBLISHER: American Association of Neurological Surgeons

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The aim of this study was to further investigate **dendritic** cell (**DC**)-based immunotherapy for malignant glioma to improve its therapeutic efficacy. **Dendritic** cells were isolated from the bone marrow and pulsed with phosphate-buffered saline, tumor RNA, tumor lysate, **Semliki Forest** virus (SFV)-LacZ, SFV-mediated B16 complementary (c)DNA, or SFV-mediated 203 glioma cDNA, resp., to treat mice bearing tumors of the 203 glioma cell line. The results indicated that pre-immunization with DCs pulsed with the same type of cDNA as in the tumor by a self-replicating RNA vector (i.e., SFV) protected mice from tumor challenge, and that therapeutic immunization prolonged the survival of mice with established tumors. The SFV induced apoptosis in DCs and their death facilitated the uptake of apoptotic cells by other DCs, thus providing a potential mechanism for enhanced immunogenicity. Conclusions. Therapy with DCs that have been pulsed with SFV-mediated tumor cDNA may be an excellent procedure for the development of new cancer vaccines.

REFERENCE COUNT: 23
REFERENCE(S):
(1) Albert, M; Nature 1998, V392, P86 CAPLUS
(2) Ashley, D; J Exp Med 1997, V186, P1177 CAPLUS
(3) Boczkowski, D; J Exp Med 1996, V184, P465 CAPLUS
(4) Celluzzi, C; J Exp Med 1996, V183, P283 CAPLUS
(5) Engelhardt, J; Hum Gene Ther 1993, V4, P759 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 8 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2001:168165 CAPLUS
DOCUMENT NUMBER: 134:217978
TITLE: Antibody-dependent enhancement of **alphavirus** vector transfection
INVENTOR(S): MacDonald, Gene H.; Johnston, Robert E.
PATENT ASSIGNEE(S): University of North Carolina at Chapel Hill, USA
SOURCE: PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001016343	A1	20010308	WO 2000-US23845	20000830

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-151718 P 19990831
US 2000-177435 P 20000121

AB The present invention provides compns. and methods for delivering a nucleotide sequence to a cell using an **alphavirus** vector that is complexed with an enhancing antibody that specifically binds to the **alphavirus** vector. Venezuelan Equine Encephalitis vectors are preferred. The cell may be a cell in vitro or in vivo. Alternatively, the cell may be removed from a subject, administered the **alphavirus** vector ex vivo and then administered to a

subject. Antigen-presenting cells are preferred, with **dendritic** cells being more preferred. Also provided are methods of producing an immune response in a subject, e.g., for producing an immune response against an antigen assocd. with a pathogen or for immunotherapy of cancer of tumors.

REFERENCE COUNT: 4

REFERENCE(S):
(1) Akzo Nobel Nv; EP 0659885 A 1995 CAPLUS
(2) Anon; http://wwwamb.casaccia.enea.it/glc/CD-table.htm 1995
(3) Linn, M; J GEN VIROL 1996, V77, P407 CAPLUS
(4) Univ North Carolina; WO 9532733 A 1995 CAPLUS

L6 ANSWER 9 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2001:135251 CAPLUS

DOCUMENT NUMBER: 134:294223

TITLE: Enhancement of **Sindbis** virus self-replicating RNA vaccine potency by targeting antigen to endosomal/lysosomal compartments

AUTHOR(S): Cheng, Wen-Fang; Hung, Chien-Fu; Hsu, Keng-Fu; Chai, Chee-Yin; He, Liangmei; Ling, Morris; Slater, Leigh A.; Roden, Richard B. S.; Wu, T.-C.

CORPORATE SOURCE: Department of Pathology, Johns Hopkins Medical Institutions, Baltimore, MD, 21205, USA

SOURCE: Hum. Gene Ther. (2001), 12(3), 235-252
CODEN: HGTHE3; ISSN: 1043-0342

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Self-replicating RNA vaccines (RNA replicons) have emerged as an attractive approach for tumor immunotherapy. RNA replicons do not integrate into host chromosomes, eliminating the concern for oncogenicity assocd. with a DNA vaccine. In this study, the authors used human papillomavirus type 16 (HPV-16) E7 as a model antigen and evaluated E7-specific immunity generated by a **Sindbis** virus self-replicating RNA vector, SIN-rep5. Three different constructs were created to target E7 antigen to different cellular localizations: (1) E7, a cytosolic/nuclear protein; (2) Sig/E7, a secretory protein; (3) Sig/E7/LAMP-1, in which the authors linked the transmembrane and cytoplasmic regions of the lysosome-assocd. membrane protein 1 (LAMP-1) to E7 protein to target E7 to the endosomal/lysosomal compartment. The authors found that the RNA replicon vaccine contg. the Sig/E7/LAMP-1 fusion gene generated the highest E7-specific T cell-mediated immune responses and antitumor effects relative to RNA vaccines contg. either wild-type E7 or Sig/E7. Our in vitro studies demonstrated that E7 antigen from

Sig/E7/LAMP-1 RNA replicon-transfected apoptotic cells can be taken up by bone marrow-derived **dendritic** cells (**DCs**) and presented more efficiently through the MHC class I pathway than wild-type E7 RNA replicon-transfected apoptotic cells. Furthermore, the authors' data revealed that CD8+ T cells, CD4+ T cells, and NK cells were important for the antitumor effects generated by Sig/E7/LAMP-1 RNA vaccination. These results indicate that targeting antigen to the endosomal/lysosomal compartment via fusion to LAMP-1 may greatly enhance the potency of self-replicating RNA vaccines.

REFERENCE COUNT: 44

REFERENCE(S):
(1) Albert, M; J Exp Med 1998, V188, P1359 CAPLUS
(2) Albert, M; Nature 1998, V392, P86 CAPLUS
(3) Berglund, P; AIDS Res Hum Retroviruses 1997, V13, P1487 CAPLUS
(4) Berglund, P; Nat Biotechnol 1998, V16, P562 CAPLUS
(5) Bigger, J; J Immunol 1998, V160, P5826 CAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 10 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:742266 CAPLUS

DOCUMENT NUMBER: 133:320989

TITLE: Compositions and methods for generating an immune response utilizing **alphavirus** -based vector systems

INVENTOR(S): Polo, John M.; Dubensky, Thomas W., Jr.; Frolov, Ilya; Gardner, Jason P.; Otten, Gillis; Barnett, Susan; Driver, David A.

PATENT ASSIGNEE(S): Chiron Corporation, USA

SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061772	A2	20001019	WO 2000-US10722	20000414
WO 2000061772	A3	20010208		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,

US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-129498 P 19990414
US 1999-148086 P 19990809
US 2000-191363 P 20000322

AB Methods are provided for generating immune responses utilizing **alphavirus**-based vector systems. Thus, **Sindbis** virus is passaged 4 times in primary human **dendritic** cells obtained from different donors, with intermediate plaque purifn. in 293 and BHK-21 cells. The resulting viral strains infect human **dendritic** cells, primarily as a result of an amino acid substitution at residue 160 of the E2 glycoprotein as compared to the wild type. Other similar **alphavirus**-based systems, such as **Semliki Forest** virus, **Venezuelan equine** encephalitis **virus**, and **Ross River** virus, also may be readily substituted. Eukaryotic layered vector initiation systems (ELVIS) are provided comprising a 5' promoter capable of initiating in vivo the 5' synthesis of **alphavirus** RNA from cDNA, a sequence which initiates transcription of **alphavirus** RNA following the 5'-promoter, a nucleic acid mol. which operably encodes all 4 alphaviral nonstructural proteins, an **alphavirus** RNA polymerase recognition sequence, and a 3' polyadenylate tract. The nonstructural proteins contain a mutation in at lease one of residues 346, 441, or 473 in nsP1; residues 438, 622, 634, or 715 in nsP2; residues 417, 456, or 505 in nsP3, and residues 266 in nsP4. The construction of a full-length cDNA clone, replicon vectors, and structural protein expression (packaging) cassettes from a human **dendritic** cell adapted **alphavirus**, such as SinDCchiron virus, is readily accomplished. A wide variety of therapeutic proteins and antigens may be expressed from the **alphavirus**-based vector systems, as demonstrated using the HIV gag polypeptide as an example antigen.

L6 ANSWER 11 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:727180 CAPLUS
DOCUMENT NUMBER: 134:264711
TITLE: **Alphavirus** DNA and particle replicons for vaccines and gene therapy
AUTHOR(S): Polo, J. M.; Gardner, J. P.; Ji, Y.; Belli, B. A.; Driver, D. A.; Sherrill, S.; Perri, S.; Liu, M. A.; Dubensky, T. W., Jr.
CORPORATE SOURCE: Vaccines & Gene Therapy, Emeryville, CA, USA
SOURCE: Dev. Biol. (2000), 104(Development and Clinical Progress of DNA Vaccines), 181-185
CODEN: DBEIAI; ISSN: 1424-6074

PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 15 refs. **Alphaviruses** have several features that make them attractive as gene delivery platforms, and vectors derived principally from **Sindbis** virus (SIN), **Semliki Forest** virus (SFV), and **Venezuelan equine** encephalitis **virus** (VEE), are currently being developed as prophylactic and therapeutic vaccines for infectious diseases and cancer. **Alphavirus** vectors, termed "replicons", retain the nonstructural protein genes encoding the viral replicase, that in turn program high level cytoplasmic amplification of the vector RNA. We have developed plasmid DNA and recombinant vector particle delivery systems derived from the prototype **alphavirus**, SIN. Each system uses RNA polymerase II-based expression of **alphavirus** genome components and both vector formats are highly efficacious towards inducing robust antigen-specific immune responses in vaccinated animals. To increase the potency of SIN vector particles, which are not known to be lymphotropic, the tropism was re-directed for efficient infection of **dendritic** cells, both in vitro and in vivo.
REFERENCE COUNT: 15
REFERENCE(S): (1) Berglund, P; Nature Biotech 1998, V16, P562 CAPLUS
(2) Cella, M; J Exp Med 1999, V189, P821 CAPLUS
(3) Dubensky, T; J Virol 1996, V70, P508 CAPLUS
(4) Frolov, I; J Virol 1994, V68, P1721 CAPLUS
(5) Frolov, I; J Virol 1997, V71, P2819 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 12 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:457216 CAPLUS
DOCUMENT NUMBER: 133:100437
TITLE: Polynucleotides encoding antigenic HIV type C Gag- and/or Env-containing polypeptides for AIDS vaccine development
INVENTOR(S): Barnett, Susan; Zur, Megede Jan
PATENT ASSIGNEE(S): Chiron Corp., USA
SOURCE: PCT Int. Appl., 113 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2000039304 A2 20000706 WO 1999-US31273 19991230
WO 2000039304 A3 20010118
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-114495 P 19981231
US 1999-152195 P 19990901

AB The present invention relates to polynucleotides encoding immunogenic HIV type C Gag- and/o6r Env-contg. polypeptides which can be used as AIDS vaccines. The coding sequences of HIV-1 Env, Gag, Gag-protease and Gag-polymerase, and some inhibitory (or instability) elements (INS) located within these coding sequences are modified to construct more efficient expression vectors. Methods of generation of packaging cell lines, and prodn. of Gag- and/or Env-contg. proteins, analyzing the synthetic gene expression, immunizing animals with the **Sindbis** virus expression constructs, and evaluating their immunogenicity are described.

L6 ANSWER 13 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:431421 CAPLUS
TITLE: Langerhans cells migrate to local lymph nodes following cutaneous infection with an arbovirus
AUTHOR(S): Johnston, Linda J.; Halliday, Gary M.; King, Nicholas J. C.
CORPORATE SOURCE: Departments of Pathology, University of Sydney, Sydney, 2006, Australia
SOURCE: J. Invest. Dermatol. (2000), 114(3), 560-568
CODEN: JIDEAE; ISSN: 0022-202X
PUBLISHER: Blackwell Science, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Whereas there has been recent interest in interactions between **dendritic** cells and pathogenic viruses, the role of **dendritic** cells in the initiation of protective immunity to such organisms has not been elucidated. The aim of this study was to examine whether a resident **dendritic** cell population in the skin, Langerhans cells, respond to cutaneous viral infections which are effectively cleared by the immune system. We therefore characterized the ability of Langerhans cells to migrate to local draining lymph nodes following infection with the arthropod-borne viruses, West Nile virus or **Semliki Forest** virus. The data show that major histocompatibility complex class

II+/NLDC145+/E-cadherin+ Langerhans cell nos. are increased in the draining lymph nodes of infected mice and this increase is accompanied by a concomitant decrease in the Langerhans cell d. in the epidermis. Langerhans cell migration is assocd. with an accumulation of leukocytes in the lymph node, which is one of the earliest events in the initiation of an immune response. Both the migratory response and the draining lymph node leukocyte accumulation were abrogated if UV-inactivated instead of live viruses were used, suggesting the activation and subsequent migration of Langerhans cells requires a live, replicating antigen. Our findings are likely to have wider implications for the development of epidermally delivered vaccines and suggest that mobilization of **dendritic** cells may be involved in the development of immune responses to arthropod-borne viruses.

REFERENCE COUNT: 51
REFERENCE(S):
(1) Aiba, S; J Immunol 1990, V145, P2791 CAPLUS
(2) Aiba, S; J Invest Dermatol 1993, V100, P143 CAPLUS
(3) Becker, Y; Virus Genes 1995, V9, P133 CAPLUS
(4) Blacklaws, B; J Virol 1995, V69, P1400 CAPLUS
(5) Borkowski, T; Eur J Immunol 1994, V24, P2767 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 14 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:402017 CAPLUS
DOCUMENT NUMBER: 133:54574
TITLE: Recombinant vectors expressing multiple costimulatory molecules, host cell infection, and uses in immunogenic applications
INVENTOR(S): Schlom, Jeffrey; Hodge, James; Panicali, Dennis
PATENT ASSIGNEE(S): United States Dept. of Health and Human Services, USA; Therion Biologics Corporation
SOURCE: PCT Int. Appl., 188 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000034494	A1	20000615	WO 1999-US26866	19991112

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,

SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-111582 P 19981209

AB The present invention provides recombinant vectors encoding and expressing at least three or more costimulatory mols and host cells infected by the vector. The recombinant vector may addnl. contain a gene encoding one or more target antigens or immunol. epitope as well as cytokine, chemokine, or Flt-3L. A method of making a recombinant poxvirus, of enhancing an immune response of an individual by administering a recombinant vector, and of treating or preventing a disease by activating a T lymphocyte, are also presented. Further describes are a method of making a progenitor **dendritic** cell or **dendritic** cell, of assesing the efficacy of a vaccine against a target antigen, and of screening for novel immunogenic peptides. The synergistic effect of these costimulatory mols. on the enhanced activation of T cells was demonstrated. The degree of T-cell activation using recombinant vectors contg. genes encoding three costimulatory mols. was far greater than the sum of recombinant vector constructs contg. one costimulatory mol. and greater than the use of two costimulatory mols. Results employing the triple costimulatory vectors were most dramatic under conditions of either low levels of first signal or low stimulator to T-cell ratios. This phenomenon was obsd. with both isolated CD4+ and CD8+ T cells. The recombinant vectors of the present invention are useful as immunogenes and vaccines against cancer and pathogenic micro-organisms, and in providing host cells, including **dendritic** cells and splenocytes with enhanced antigen-presenting functions.

REFERENCE COUNT: 4

REFERENCE(S):
(1) Hodge, J; Cancer Res 1999, V59, P5800 CAPLUS
(2) Keting, C; US 5738852 A 1998 CAPLUS
(3) Therion Biolog Corp; WO 9804727 A 1998 CAPLUS
(4) US Health; WO 9610419 A 1996 CAPLUS

L6 ANSWER 15 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 2000:254039 CAPLUS

DOCUMENT NUMBER: 132:289590

TITLE: Peptide-enhanced cationic lipid transfections

INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Schifferli, Kevin P.; Gebeyehu, Gulilat

PATENT ASSIGNEE(S): Life Technologies, Inc., USA

SOURCE: U.S., 103 pp., Cont.-in-part of U.S. 5,736,392. CODEN: USXXAM

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6051429	A	20000418	US 1997-818200	19970314
US 5736392	A	19980407	US 1996-658130	19960604
WO 9840502	A1	19980917	WO 1998-US5232	19980316
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9865622	A1	19980929	AU 1998-65622	19980316
EP 1007699	A1	20000614	EP 1998-911737	19980316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:
US 1995-477354 B2 19950607
US 1996-658130 A2 19960604
US 1997-818200 A 19970314
WO 1998-US5232 W 19980316

AB The present invention provides compns. useful for transfecting eukaryotic cells comprising nucleic acid complexes with peptides, wherein the peptide is optionally covalently coupled to a nucleic acid-binding group, and cationic lipids or dendrimers as transfection agents. The invention also provides transfection compns. in which a peptide is covalently linked to the transfection agent (lipid, cationic lipid or dendrimer). Inclusion of peptides or modified-peptides in transfection compns. or covalent attachment of peptides to transfection agents results in enhanced transfection efficiency. Methods for the prepn. of transfection compns. and methods of using these transfection compns. as intracellular delivery agents and extracellular targeting agents are also disclosed.

REFERENCE COUNT: 46
REFERENCE(S):
(2) Anon; EP 0359347 1990 CAPLUS
(4) Anon; EP 0544292 1992 CAPLUS
(5) Anon; WO 9213570 1992 CAPLUS
(7) Anon; WO 9307282 1993 CAPLUS
(8) Anon; WO 9307283 1993 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 16 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:183080 CAPLUS
DOCUMENT NUMBER: 132:320767
TITLE: Alpha/Beta interferon protects adult mice from fatal **Sindbis** virus infection and is an important determinant of cell and tissue tropism
AUTHOR(S): Ryman, Kate D.; Klimstra, William B.; Nguyen, Khuong B.; Biron, Christine A.; Johnston, Robert E.
CORPORATE SOURCE: Department of Microbiology and Immunology, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: J. Virol. (2000), 74(7), 3366-3378
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Infection of adult 129 Sv/Ev mice with consensus **Sindbis** virus strain TR339 is subclin. due to an inherent restriction in early virus replication and viremic dissemination. By comparing the pathogenesis of TR339 in 129 Sv/Ev mice and .alpha./.beta. interferon receptor null (IFN-.alpha./.beta.R-/-) mice, the authors have assessed the contribution of IFN-.alpha./.beta. in restricting virus replication and spread and in detg. cell and tissue tropism. In adult 129 Sv/Ev mice, s.c. inoculation with 100 PFU of TR339 led to extremely low-level virus replication and viremia, with clearance under way by 96 h postinoculation (p.i.). In striking contrast, adult IFN-.alpha./.beta.R-/- mice inoculated s.c. with 100 PFU of TR339 succumbed to the infection within 84 h. By 24 h p.i. a high-titer serum viremia had seeded infectious virus systemically, coincident with the systemic induction of the proinflammatory cytokines interleukin-12 (IL-12) p40, IFN-.gamma., tumor necrosis factor .alpha., and IL-6. Replicating virus was located in macrophage-**dendritic** cell (**DC**)-like cells at 24 h p.i. in the draining lymph node and in the splenic marginal zone. By 72 h p.i. virus replication was widespread in macrophage-DC-like cells in the spleen, liver, lung, thymus, and kidney and in fibroblast-connective tissue and periosteum, with sporadic neuroinvasion. IFN-.alpha./.beta.-mediated restriction of TR339 infection was mimicked in vitro in peritoneal exudate cells from 129 Sv/Ev vs. IFN-.alpha./.beta.R-/- mice. Thus, IFN-.alpha./.beta. protects the normal adult host from viral infection by rapidly conferring an antiviral state on otherwise permissive cell types, both locally and systemically. Ablation of the IFN-.alpha./.beta. system alters the apparent cell and tissue tropism of the virus and renders macrophage-DC-lineage cells permissive to infection.

REFERENCE COUNT: 65

REFERENCE(S):

(3) Biron, C; Curr Opin Microbiol 1999, V2, P374 CAPLUS
(5) Cella, M; J Exp Med 1999, V189, P821 CAPLUS
(6) Charles, P; Virology 1995, V208, P662 CAPLUS
(7) Ciavarra, R; J Immunol 1997, V158, P1749 CAPLUS
(8) Cousens, L; J Exp Med 1999, V189, P1315 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 17 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:141420 CAPLUS
TITLE: Papers to Appear in Forthcoming Issues
AUTHOR(S): Anon.
SOURCE: Cell. Immunol. (2000), 199(2), 138
CODEN: CLIMB8; ISSN: 0008-8749
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal; Miscellaneous
LANGUAGE: English
AB (Received and Accepted Dates Follow Title)Regulation of CS1 Fibronectin Expression and Function by IL-1 in Endothelial Cells. David L. Boyle, Yan Shi, Steffen Gay, and Gary S. Firestein. (Received 7/23/99; accepted 1/5/00.)The Autoimmune Accelerating Yaa Mutation Does Not Accelerate Murine AIDS. Ambros W. Hugin, Liliane Fossati-Jimack, and Shozo Izui. (Received 8/18/99; accepted 1/5/00.)Lectin Ligands on Human **Dendritic** Cells and Identification of a Peanut Agglutinin Pos. Subset in Blood. H. Sherbini, B. Hock, D. Fearnley, A. McLellan, S. Vuckovic, and D. N. J. Hart. (Received 9/9/99; accepted 1/5/00.)B Cells and Antibodies in the Pathogenesis of Myelin Injury in **Semliki Forest** Virus Encephalomyelitis. Tamar A. Smith-Norowitz, Raymond A. Sobel, and Foroozan Mokhtarian. (Received 9/24/99; accepted 1/5/00.)The CD40-Inducible Bcl-2 Family Member A1 Protects B Cells from Antigen Receptor-Mediated Apoptosis. Andrew Craxton, Peter I. Chuang, Geraldine Shu, John M. Harlan, and Edward A. Clark. (Received 12/13/99; accepted 1/9/00.)In Vitro Characterization of Five Humanized OKT3 Effector Function Variant Antibodies. Danlin Xu, Maria-Luisa Alegre, Sally S. Varga, Annette L. Rothermel, Alexander M. Collins, Virginia L. Pulito, Lewis S. Hanna, Kevin P. Dolan, Paul W. H. I. Parren, Jeffrey A. Bluestone, Linda K. Jolliffe, and Robert A. Zivin. (Received 8/12/99; accepted 1/10/00.)Differential Control of Neonatal Tolerance by Antigen Dose vs. Extended Exposure and Adjuvant. Booki Min, Kevin L. Legge, Jacque C. Caprio, Lequn Li, Randal Gregg, and Habib Zaghouani. (Received 9/29/99; accepted 1/10/00.). (c) 2000 Academic Press.

L6 ANSWER 18 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:116156 CAPLUS

DOCUMENT NUMBER: 132:263829
TITLE: Stimulation of cytotoxic T cells against idiotype immunoglobulin of malignant lymphoma with protein-pulsed or idiotype-transduced **dendritic** cells
AUTHOR(S): Osterroth, Frank; Garbe, Annette; Fisch, Paul; Veelken, Hendrik
CORPORATE SOURCE: Departments of Hematology/Oncology and Pathology, Freiburg University Medical Center, Freiburg, D-79106, Germany
SOURCE: Blood (2000), 95(4), 1342-1349
CODEN: BLOOAW; ISSN: 0006-4971
PUBLISHER: American Society of Hematology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Because of their hypervariable regions and somatic mutations, the antigen receptor mols. of lymphomas (idiotypes) are tumor-specific antigens and attractive targets for anti-lymphoma immunotherapy. For the optimal induction of human idiotype-specific cytotoxic T cells (CTL), idiotype was presented to CD8+ peripheral blood mononuclear cells by monocyte-derived autologous **dendritic** cells (**DC**) after the endocytosis of idiotype protein or by idiotype-expressing **DC**. Recombinant idiotype was obtained as a functionally folded Fab fragment by periplasmic expression in Escherichia coli. Idiotype-expressing DC were generated by transduction with recombinant **Semliki forest** virus vectors encompassing heavy- or light-chain idiotype genes. Autologous lymphoblastoid cell lines stably transfected with Epstein-Barr virus-based idiotype expression vectors were used as target cells to detect idiotype-specific lysis. CTL stimulated with idiotype-loaded DC showed strong specific, CD8-mediated, and major histocompatibility complex (MHC) class I-restricted cytotoxicity against autologous heavy- and light-chain idiotype. In contrast, stimulation with idiotype-transduced DC resulted in only moderate natural killer cell activity. These data confirm the existence of idiotype-specific CTL in patients with lymphoma, define a "good manufg. practice" -compatible protocol for the generation of these cells without the requirement of viable lymphoma cells, and favor the processing of exogenous antigen over DC transduction for the induction of MHC I-restricted CTL against idiotypes with unknown antigenicity.
REFERENCE COUNT: 43
REFERENCE(S):
(1) Banchereau, J; Nature 1998, V392, P245 CAPLUS
(3) Boon, T; J Exp Med 1996, V183, P725 CAPLUS
(5) Cella, M; Curr Opin Immunol 1997, V9, P10 CAPLUS
(7) Fernandez, N; Nat Med 1999, V5, P405 CAPLUS

(8) Fields, P; J Mol Med 1996, V74, P673 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 19 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:42478 CAPLUS
TITLE: Role of **dendritic** cell targeting in **venezuelan equine** encephalitis **virus** pathogenesis
AUTHOR(S): MacDonald, Gene H.; Johnston, Robert E.
CORPORATE SOURCE: Department of Microbiology and Immunology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, 27599-7290, USA
SOURCE: J. Virol. (2000), 74(2), 914-922
CODEN: JOVIAM; ISSN: 0022-538X
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The initial steps of **Venezuelan equine** encephalitis **virus** (VEE) spread from inoculation in the skin to the draining lymph node have been characterized. By using green fluorescent protein and immunocytochem., **dendritic** cells in the draining lymph node were detd. to be the primary target of VEE infection in the first 48 h following inoculation. VEE viral replicon particles, which can undergo only one round of infection, identified Langerhans cells to be the initial set of cells infected by VEE directly following inoculation. These cells are resident **dendritic** cells in the skin, which migrate to the draining lymph node following activation. A point mutation in the E2 glycoprotein gene of VEE that renders the virus avirulent and compromises its ability to spread beyond the draining lymph blocked the appearance of virally infected **dendritic** cells in the lymph node in vivo. A second-site suppressor mutation that restores viral spread to lymphoid tissues and partially restore virulence likewise restored the ability of VEE to infect **dendritic** cells in vivo.
REFERENCE COUNT: 35
REFERENCE(S): (1) Banchereau, J; Nature 1998, V392, P245 CAPLUS
(2) Bhardwaj, N; J Exp Med 1997, V186, P795 CAPLUS
(3) Borrow, P; J Virol 1995, V69, P1059 CAPLUS
(4) Caley, I; J Virol 1997, V71, P3031 CAPLUS
(5) Charles, P; Virology 1995, V208, P662 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 20 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 2000:29999 CAPLUS

DOCUMENT NUMBER: 132:333014
TITLE: DNA and RNA-based vaccines: principles, progress and prospects
AUTHOR(S): Leitner, Wolfgang W.; Ying, Han; Restifo, Nicholas P.
CORPORATE SOURCE: National Cancer Institute, National Institutes of Health, Bethesda, MD, 20892-1502, USA
SOURCE: Vaccine (1999), 18(9-10), 765-777
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 42 refs. DNA vaccines were introduced less than a decade ago but have already been applied to a wide range of infectious and malignant diseases. Here we review the current understanding of the mechanisms underlying the activities of these new vaccines. We focus on recent strategies designed to enhance their function including the use of immunostimulatory (CpG) sequences, **dendritic** cells (**DC**), co-stimulatory mols. and cytokine- and chemokine-adjuvants. Although genetic vaccines have been significantly improved, they may not be sufficiently immunogenic for the therapeutic vaccination of patients with infectious diseases or cancer in clin. trials. One promising approach aimed at dramatically increasing the immunogenicity of genetic vaccines involves making them "self-replicating". This can be accomplished by using a gene encoding RNA replicase, a polyprotein derived from **alphaviruses**, such as **Sindbis** virus. Replicase-contg. RNA vectors are significantly more immunogenic than conventional plasmids, immunizing mice at doses as low as 0.1 .mu.g of nucleic acid injected once i.m. Cells transfected with "self-replicating" vectors briefly produce large amts. of antigen before undergoing apoptotic death. This death is a likely result of requisite double-stranded (ds) RNA intermediates, which also have been shown to super-active DC. Thus, the enhanced immunogenicity of "self-replicating" genetic vaccines may be a result of the prodn. of pro-inflammatory dsRNA, which mimics an RNA-virus infection of host cells.
REFERENCE COUNT: 142
REFERENCE(S):
(1) Albert, M; Nature 1998, V392, P86 CAPLUS
(2) Barry, M; Vaccine 1997, V15, P788 CAPLUS
(3) Bell, A; Virology 1997, V232, P241 CAPLUS
(4) Berglund, P; Nat Biotech 1998, V16, P562 CAPLUS
(5) Berglund, P; Trends Biotechnol 1996, V14, P130 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 21 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:659264 CAPLUS
DOCUMENT NUMBER: 131:285394
TITLE: Methods and modified cells for the treatment of cancer
INVENTOR(S): MacDonald, Gene H.; Martin, Brian K.; Johnston, Robert E.; Ting, Jenny P-y
PATENT ASSIGNEE(S): University of North Carolina at Chapel Hill, USA; Ting, Jenny P.-Y.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951263	A2	19991014	WO 1999-US7704	19990408
WO 9951263	A3	20000203		
W: AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, EE, ES, FI, FI, GB, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9937440	A1	19991025	AU 1999-37440	19990408
EP 1069908	A2	20010124	EP 1999-919803	19990408
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1998-81092 P 19980408
WO 1999-US7704 W 19990408

AB The present invention provides methods of preventing and/or treating cancers (including tumors). In one preferred embodiment, the invention is practiced to induce regression of an existing cancer or tumor and/or to prevent metastasis and/or to prevent growth of metastatic nodules. In other preferred embodiments, the invention may be used as a prophylaxis to prevent the development of primary cancers through a childhood or adult vaccination program against specific tumor antigens for cancers with high incidences. In an alternate preferred embodiment, the present invention provides methods of establishing an immune response against a universal artificial tumor antigen through a childhood or adult vaccine program, thus providing a long-term immune response that can be utilized at any point to treat any cancer which develops later in

life. The present invention also provides cancer and tumor cells stably expressing an artificial antigen, preferably an artificial cell-surface antigen.

L6 ANSWER 22 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:461772 CAPLUS
DOCUMENT NUMBER: 131:209757
TITLE: Recombinant **Semliki Forest** virus and **Sindbis** virus efficiently infect neurons in hippocampal slice cultures
AUTHOR(S): Ehrengruber, Markus U.; Lundstrom, Kenneth; Schweitzer, Christophe; Heuss, Christian; Schlesinger, Sondra; Gahwiler, Beat H.
CORPORATE SOURCE: Brain Research Institute, University of Zurich, Zurich, CH-8057, Switz.
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1999), 96(12), 7041-7046
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Gene transfer into nervous tissue is a powerful tool for the anal. of gene function. By using a rat hippocampal slice culture prepn., we show here that **Semliki Forest** virus (SFV) and **Sindbis** virus (SIN) vectors are useful for the effective infection of neurons. The stratum pyramidale and/or the granular cell layer were injected with recombinant virus encoding .beta.-galactosidase (LacZ) or green fluorescent protein (GFP). By using low concns. of injected SFV-LacZ or SIN-LacZ, we detected LacZ staining of pyramidal cells, interneurons, and granule cells. About 60% of the infected cells showed clear neuronal morphol.; thus, relatively few glial cells expressed the transgene. Expression of GFP from SFV and SIN vectors gave similar results, with an even higher percentage (>90%) of the GFP-pos. cells identified as neurons. Infected pyramidal cells were readily recognized in living slices, displaying GFP fluorescence in **dendrites** of up to fourth order and in **dendritic** spines. They appeared morphol. normal and viable at 1-5 days postinfection. We conclude that both SFV and SIN vectors efficiently transfer genes into neurons in hippocampal slice cultures. In combination with the GFP reporter, SFV and SIN vectors will allow the physiol. examn. of identified neurons that have been modified by overexpression or suppression of a specific gene product.
REFERENCE COUNT: 38
REFERENCE(S): (1) Ankarcrona, M; Neuron 1995, V15, P961 CAPLUS
(3) Berglund, P; Biotechnology 1993, V11, P916 CAPLUS
(4) Bredenbeek, P; J Virol 1993, V67, P6439

CAPLUS
(6) Davis, N; Proc Natl Acad Sci USA 1986, V83, P6771 CAPLUS
(8) Ehrengruber, M; Methods Enzymol 1998, V293, P483 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 23 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:444820 CAPLUS
DOCUMENT NUMBER: 131:198315
TITLE: Cancer therapy using a self-replicating RNA vaccine
AUTHOR(S): Ying, Han; Zaks, Tal Z.; Wang, Rong-Fu; Irvine, Kari R.; Kammula, Udai S.; Marincola, Francesco M.; Leitner, Wolfgang W.; Restifo, Nicholas P.
CORPORATE SOURCE: Surgery Branch, National Cancer Institute, Bethesda, MD, 20892-1502, USA
SOURCE: Nat. Med. (N. Y.) (1999), 5(7), 823-827
CODEN: NAMEFI; ISSN: 1078-8956
PUBLISHER: Nature America
DOCUMENT TYPE: Journal
LANGUAGE: English

AB 'Naked' nucleic acid vaccines are potentially useful candidates for the treatment of patients with cancer, but their clin. efficacy has yet to be demonstrated. We sought to enhance the immunogenicity of a nucleic acid vaccine by making it 'self-replicating'. We accomplished this by using a gene encoding an RNA replicase polyprotein derived from the **Semliki forest** virus, in combination with a model antigen. A single i.m. injection of a self-replicating RNA immunogen elicited antigen-specific antibody and CD8+ T-cell responses at doses as low as 0.1 .mu.g. Pre-immunization with a self-replicating RNA vector protected mice from tumor challenge, and therapeutic immunization prolonged the survival of mice with established tumors. The self-replicating RNA vectors did not mediate the prodn. of substantially more model antigen than a conventional DNA vaccine did in vitro. However, the enhanced efficacy in vivo correlated with a caspase-dependent apoptotic death in transfected cells. This death facilitated the uptake of apoptotic cells by **dendritic** cells, providing a potential mechanism for enhanced immunogenicity. Naked, non-infectious, self-replicating RNA may be an excellent candidate for the development of new cancer vaccines.

REFERENCE COUNT: 23
REFERENCE(S):

(1) Albert, M; Nature 1998, V392, P86 CAPLUS
(2) Atkins, G; Mol Biotechnol 1996, V5, P33 CAPLUS
(3) Berglund, P; Nature Biotechnol 1998, V16, P562 CAPLUS

(4) Cella, M; J Exp Med 1999, V189, P821 CAPLUS
(5) Chappell, D; Cancer Res 1999, V59, P59 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 24 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1999:401694 CAPLUS
DOCUMENT NUMBER: 131:43583
TITLE: **Venezuelan equine** encephalitis **virus** vectors expressing tumor-associated antigens to induce cancer immunity
INVENTOR(S): Hippenmeyer, Paul J.
PATENT ASSIGNEE(S): G.D. Searle & Co., USA
SOURCE: PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9930734	A1	19990624	WO 1998-US25725	19981214
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9917106	A1	19990705	AU 1999-17106	19981214
EP 1039926	A1	20001004	EP 1998-961904	19981214
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-68080 P 19971218
WO 1998-US25725 W 19981214

AB The present invention describes a novel method of inducing immunity to cancer. This invention further discloses the use of Venezuelan Equine Encephalitis (VEE) virus vectors for expression of tumor-assocd. antigens, tumor-assocd. antigenic peptides and cytokines and methods for expressing these heterologous products in cultured cells, and in humans or animals.

REFERENCE COUNT: 9
REFERENCE(S): (1) Brossart, P; J IMMUNOL 1997, V158, P3270 CAPLUS

(3) Sidney, J; WO 9504542 A 1995 CAPLUS
(4) Sloan Kettering Inst Cancer; WO 9520974 A 1995 CAPLUS
(5) Tuting, T; JOURNAL OF IMMUNOLOGY 1998, V160(3), P1139 CAPLUS
(6) Tuting, T; JOURNAL OF MOLECULAR MEDICINE 1997, V75(7), P478 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 25 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:709094 CAPLUS
DOCUMENT NUMBER: 129:326928
TITLE: Bifunctional proteins for cell-specific viral vector targeting
INVENTOR(S): Young, John; Snitkovsky, Sophie
PATENT ASSIGNEE(S): President and Fellows of Harvard College, USA
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9847916	A1	19981029	WO 1998-US7720	19980416
W: AU, CA, JP, NZ, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9871277	A1	19981113	AU 1998-71277	19980416

PRIORITY APPLN. INFO.: US 1997-844359 19970418
WO 1998-US7720 19980416

AB The invention relates to a novel bifunctional mol. comprising a first binding moiety which binds to a surface mol. on a target cell and a second binding moiety which binds to a surface mol. on a viral vector. The bifunctional mol. targets the viral vector to the target cell with improved infectivity and selectivity. The mol. can be used, for example, in in vitro and in vivo gene delivery methods. Thus, a recombinant protein comprising epidermal growth factor fused to an Env protein-binding domain was used to target avian leukosis virus to EGF receptor-expressing cells.

L6 ANSWER 26 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:621324 CAPLUS
DOCUMENT NUMBER: 129:240848
TITLE: Increasing the efficiency of uptake of transforming DNA complexes with polycations using peptides

INVENTOR(S): Hawley-Nelson, Pamela; Lan, Jianqing; Shih, Pojen; Jessee, Joel A.; Ciccarone, Valentina C.; Evans, Krista L.; Schifferli, Kevin P.; Gebeyehu, Guililat
PATENT ASSIGNEE(S): Life Technologies, Inc., USA
SOURCE: PCT Int. Appl., 105 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9840502	A1	19980917	WO 1998-US5232	19980316
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 6051429	A	20000418	US 1997-818200	19970314
AU 9865622	A1	19980929	AU 1998-65622	19980316
EP 1007699	A1	20000614	EP 1998-911737	19980316
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.:
US 1997-818200 A 19970314
US 1995-477354 B2 19950607
US 1996-658130 A2 19960604
WO 1998-US5232 W 19980316

AB A method of increasing the efficiency of transformation of eukaryotic cells using complexes of nucleic acids with polycations is decribed. The method uses peptide conjugates with nucleic acid-binding moieties, cationic lipids and dendrimers to complex the DNA. The peptides may be synthetic or derived from a cellular protein and may be further derivatized, e.g. by selective deprotection. The peptide may also be covalently linked to the transfection agent (lipid, cationic lipid or dendrimer). Inclusion of peptides or modified-peptides in transfection compns. or covalent attachment of peptides to transfection agents increases the efficiency of transfection. Methods for the prepn. of transfection compns. and methods of using these transfection compns. as intracellular delivery agents and extracellular targeting agents are also disclosed.

L6 ANSWER 27 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1998:381829 CAPLUS
DOCUMENT NUMBER: 129:134964
TITLE: Exogenous and endogenous IL-10 regulate IFN-.alpha. production by peripheral blood mononuclear cells in response to viral stimulation
AUTHOR(S): Payvandi, Faribourz; Amrute, Sheela; Fitzgerald-Bocarsly, Patricia
CORPORATE SOURCE: Dep. Pathol. Lab. Med., Graduate School Biomed. Sci., Univ. Med. Dentistry/New Jersey, New Jersey Med. School, Newark, NJ, 07103, USA
SOURCE: J. Immunol. (1998), 160(12), 5861-5868
CODEN: JOIMA3; ISSN: 0022-1767
PUBLISHER: American Association of Immunologists
DOCUMENT TYPE: Journal
LANGUAGE: English

AB IL-10 is an important regulator of the prodn. of proinflammatory cytokines. Its effect on IFN-.alpha. prodn., however, has not been reported. In this study, PBMC from healthy donors were stimulated with virus in the presence of IL-10. Human IL-10 (hIL-10) caused redns. in both the frequency of IFN-.alpha.-producing cells (IPC) and bulk IFN in response to herpes simplex virus type-1 (HSV-1), Sendai virus, Newcastle disease virus, and vesicular stomatitis virus. The inhibitory effect occurred when IL-10 was added 2 or 4 h before, or 2 h poststimulation with HSV or Sendai virus, but not when added 4 h postinduction. Unlike IL-10, IL-4 did not affect the IFN-.alpha. response to HSV. However, when PBMC were induced with Sendai virus, IFN-.alpha. prodn. was also reduced by IL-4. IL-10 treatment of PBMC resulted in strong redns. in the steady state levels of both HSV- and Sendai virus-induced IFN-.alpha.1, -.alpha.2, and -.beta. mRNA as detd. by RT-PCR. IFN-.alpha. prodn. of Sendai virus occurs predominantly by monocytes, whereas most enveloped viruses stimulate low frequency "natural IFN-producing cells (NIPC)," which are thought to be **dendritic** cells. Peripheral blood **dendritic** cells were found to express the IL-10 receptor, suggesting that IL-10 may directly act on the **dendritic** IPC. Addn. of monoclonal anti-IL-10 to PBMC resulted in a significant increase in both the frequency of IPC and the amt. of secreted IFN-.alpha. in response to HSV but not Sendai virus. We conclude that human IL-10 can serve as both an endogenous and exogenous regulator of IFN-.alpha. prodn.

L6 ANSWER 28 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:643186 CAPLUS
DOCUMENT NUMBER: 125:324125
TITLE: The .beta.-amyloid domain is essential for axonal sorting of amyloid precursor protein

AUTHOR(S): Tienari, Pentti J.; De Strooper, Bart; Ikonen, Elina; Simons, Mikael; Weidemann, Andreas; Czech, Christian; Hartmann, Tobias; Ida, Nobuo; Multhaup, Gerd; et al.

CORPORATE SOURCE: Cell Biol. Programme, European Molecular Biology Lab., Heidelberg, D-69012, Germany

SOURCE: EMBO J. (1996), 15(19), 5218-5229
CODEN: EMJODG; ISSN: 0261-4189

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The authors have analyzed the axonal sorting signals of amyloid precursor protein (APP). Wild-type and mutant versions of human APP were expressed in hippocampal neurons using the **Semliki forest** virus system. The authors show that wild-type APP and mutations implicated in Alzheimer's disease and another brain .beta.-amyloidosis are sorted to the axon. By anal. of deletion mutants the authors found that the membrane-inserted APP ectodomain but not the cytoplasmic tail is required for axonal sorting. Systematic deletions of the APP ectodomain identified two regions required for axonal delivery: one encoded by exons 11-15 in the carbohydrate domain, the other encoded by exons 16-17 in the juxtamembranous .beta.-amyloid domain. Treatment of the cells with the N-glycosylation inhibitor tunicamycin induced missorting of wild-type APP, supporting the importance of glycosylation in axonal sorting of APP. The data revealed a hierarchy of sorting signals on APP: the .beta.-amyloid-dependent membrane proximal signal was the major contributor to axonal sorting, while N-glycosylation had a weaker effect. Furthermore, recessive somatodendritic signals, most likely in the cytoplasmic tail, directed the protein to the **dendrites** when the ectodomain was deleted. Anal. of delivered protein, hemagglutinin, demonstrated that only hemagglutinin formed CHAPS-insol. complexes, suggesting distinct mechanisms of axonal sorting for these two proteins. This study is the first delineation of sorting requirements of an axonally targeted protein in polarized neurons and indicates that the .beta.-amyloid domain plays a major role in axonal delivery of APP.

L6 ANSWER 29 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1996:524456 CAPLUS

DOCUMENT NUMBER: 125:164939

TITLE: Expression and analysis of presenilin 1 in a human neuronal system: Localization in cell bodies and **dendrites**

AUTHOR(S): Cook, David G.; Sung, Jane C.; Golde, Todd E.; Felsenstein, Kevin M.; Wojczyk, Boguslaw S.; Tanzi, Rudolph E.; Trojanowski, John Q.; Lee, Virginia M.-Y.; Doms, Robert W.

CORPORATE SOURCE: Dep. Pathology, Univ. Pennsylvania,

Philadelphia, PA, 19104, USA
SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1996), 93(17), 9223-9228
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Mutations in the recently identified presenilin 1 gene on chromosome 14 cause early onset familial Alzheimer disease (FAD). Here, the authors describe the expression and anal. of the protein coded by presenilin 1 (PS1) in NT2N neurons, a human neuronal model system. PS1 was expressed using recombinant **Semliki Forest** virions and detected by introduced antigenic tags or antisera to PS1-derived peptides. Immunopptn. revealed 2 major PS1 bands of approx. 43 and 50 kDa, neither of which were N-glycosylated or O-glycosylated. Immunoreactive PS1 was detected in cell bodies and **dendrites** of NT2N neurons but not in axons or on the cell surface. PS1 was also detected in BHK cells, where it was also intracellular and colocalized with calnexin, a marker for the rough endoplasmic reticulum. A mutant form of PS1 linked to FAD did not differ from the wild-type protein at the light microscopic level. The model system described here will enable studies of the function of PS1 in human neurons and the role of mutant PS1 in FAD.

L6 ANSWER 30 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1996:358345 CAPLUS
DOCUMENT NUMBER: 125:31828
TITLE: Phenotypic changes in Langerhans' cells after infection with arboviruses: a role in the immune response to epidermally acquired viral infection?
AUTHOR(S): Johnston, Linda J.; Halliday, Gary M.; King, Nicholas J. C.
CORPORATE SOURCE: Dep. Pathol. Med., Univ. Sydney, Sydney, 2006, Australia
SOURCE: J. Virol. (1996), 70(7), 4761-4766
CODEN: JOVIAM; ISSN: 0022-538X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The role of Langerhans cells (LC) in the initiation of an immune response to a viral infection remains unclear. In vivo epidermal infection with the arboviruses West Nile virus and **Semliki Forest** virus significantly increased the expression of major histocompatibility complex class II antigens, CD54, and CD80 on LC. Thus, during an epidermally acquired viral infection, local LC appear to mature to a phenotype approximating that of lymphoid **dendritic** cells. This change may be important in the activation of naive T cells and the subsequent clearance of viral infection.

L6 ANSWER 31 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:797180 CAPLUS
DOCUMENT NUMBER: 123:196271
TITLE: Intracellular routing of wild-type and mutated polymeric immunoglobulin receptor in hippocampal neurons in culture
AUTHOR(S): de Hoop, Meltsje; von Poser, Christine; Lange, Claudia; Ikonen, Elina; Hunziker, Walter; Dotti, Carlos G.
CORPORATE SOURCE: Cell Biology Program, European Molecular Biology Laboratory, Heidelberg, 69012, Germany
SOURCE: J. Cell Biol. (1995), 130(6), 1447-59
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Certain epithelial cells synthesize the polymeric Ig receptor (pIgR) to transport IgA and IgM into external secretions. In polarized epithelia, newly synthesized receptor is first delivered to the basolateral plasma membrane and is then, after binding the Ig, transcytosed to the apical plasma membrane, where the receptor-ligand complex is released by proteolytic cleavage. In a previous work (E. Ikonen, et al., 1993), the authors implied the existence of a dendro-axonal transcytotic pathway for the rabbit pIgR expressed in hippocampal neurons via the **Semliki Forest** virus (SFV) expression system. By labeling surface-exposed pIgR in live neuronal cells, the authors now show (a) internalization of the receptor from the **dendritic** plasma membrane to the **dendritic** early endosomes, (b) redistribution of the receptor from the **dendritic** to the axonal domain, (c) inhibition of this movement by brefeldin A, (BFA) and (d) stimulation by the activation of protein kinase C (PKC) via phorbol myristate acetate (PMA). In addn., the authors show that a mutant form of the receptor lacking the epithelial basolateral sorting signal is directly delivered to the axonal domain of hippocampal neurons. Although this mutant is internalized into early endosomes, no transcytosis to the **dendrites** could be obsd. In epithelial Madin-Darby Canine kidney (MDCK) cells, the mutant receptor could also be internalized into basolaterally derived early endosomes. These results suggest the existence of a dendro-axonal transcytotic pathway in neuronal cells which shares similarities with the basolateral to apical transcytosis in epithelial cells.

L6 ANSWER 32 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1995:622960 CAPLUS
DOCUMENT NUMBER: 123:53039
TITLE: Nocodazole-dependent transport, and brefeldin

A-sensitive processing and sorting, of newly synthesized membrane proteins in cultured neurons

AUTHOR(S): Cid-Arregui, Angel; Parton, Robert G.; Simons, Kai; Dotti, Carlos G.

CORPORATE SOURCE: Cell Biol. Prog., European Mol. Biol. Lab., Heidelberg, D-69012, Germany

SOURCE: J. Neurosci. (1995), 15(6), 4259-69
CODEN: JNRSDS; ISSN: 0270-6474

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The envelope glycoproteins of **Semliki Forest** virus (SFV), Vesicular Stomatitis virus (VSV), and Influenza Fowl Plague virus (FPV) are vectorially targeted in neurons to the plasma membrane of **dendrites** (SFV and VSV) and axons (FPV). To gain insight into the mechanisms responsible for such polarized delivery we have examd. the effects on neurons of nocodazole and brefeldin A (BFA), which are known to cause microtubule depolymn. and disassembly of the Golgi app., resp. Nocodazole treatment blocked transport of all viral glycoproteins to both axons and **dendrites**. BFA treatment induced disruption of the Golgi complex, including the trans-Golgi network (TGN), and tubulation of endosomes. However, the delivery of the SFV and FPV glycoproteins to the cell surface was not affected significantly by BFA, although processing and sorting were altered, as revealed by surface biotinylation and immunofluorescence microscopy of fixed nonpermeabilized cells. These results demonstrate the involvement of microtubules in axonal and **dendritic** transport of integral membrane glycoproteins, and the existence of a BFA-sensitive component in the sorting but not in the transport machinery.

L6 ANSWER 33 OF 37 CAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: 1995:548456 CAPLUS

DOCUMENT NUMBER: 122:311663

TITLE: Intracellular routing of human amyloid protein precursor: axonal delivery followed by transport to the **dendrites**

AUTHOR(S): Simons, M.; Ikonen, E.; Tienari, P. J.; Cid-Arregui, A.; Moenning, U.; Beyreuther, K.; Dotti, C. G.

CORPORATE SOURCE: Cell Biology Program, Univ. of heidelberg, Heidelberg, Germany

SOURCE: J. Neurosci. Res. (1995), 41(1), 121-8
CODEN: JNREDK; ISSN: 0360-4012

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A characteristic neuropathol. feature of Alzheimer's disease is the

cerebral deposition of amyloid plaques. These deposits contain .beta.A4 amyloid peptide, a cleavage product of the transmembrane protein amyloid protein precursor (APP). Despite numerous studies on the processing of the different APP isoforms in non-neuronal cells, little is known about its sorting and transport in neurons of the central nervous system (CNS). To analyze this question the authors expressed in cultured rat hippocampal neurons the human APP 695, tagged at its N-terminus with he myc epitope, using the **Semliki forest** virus (SFV) expression system. APP was first delivered from the cell body to the axon and later appeared also in the **dendrites**. Inhibition of protein synthesis at the time of axonal expression did not block the late appearance of the protein in the **dendrites**. An antibody directed against the myc tag, bound to the cell surface at 4.degree.C at the time of axonal APP expression, could be chased to the **dendritic** domain after subsequent incubation at 37.degree.C. These results suggest that the newly synthesized APP, after initial axonal delivery, may be transported to the **dendrites** by a transcytotic mechanism. The routing of APP in polarized neurons is different from that of polarized epithelial cells, in which the protein is delivered basolaterally, arguing for neuronal specific sorting and processing mechanisms.

L6 ANSWER 34 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1994:6446 CAPLUS
DOCUMENT NUMBER: 120:6446
TITLE: Transcytosis of the polymeric immunoglobulin receptor in cultured hippocampal neurons
AUTHOR(S): Ikonen, Elina; Parton, Robert G.; Hunziker, Walter; Simons, Kai; Dotti, Carlos G.
CORPORATE SOURCE: Cell Biol. Program, Eur. Mol. Biol. Lab., Heidelberg, D-69012, Germany
SOURCE: Curr. Biol. (1993), 3(10), 635-44
CODEN: CUBLE2; ISSN: 0960-9822
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors report expression of the polymeric Ig receptor in cultured hippocampal neurons, using a **Semliki Forest** Virus expression system, and show by immunofluorescence microscopy that the newly synthesized receptor is targeted from the Golgi complex predominantly to the **dendrites** only; .apprx.20% of the infected neurons display axonal immunofluorescence. Addn. of ligand leads to significant redistribution of the receptor to the axons, shown by an .apprx.3 fold increase in axonal immunoreactivity with the anti-receptor antibodies. Thus, a transcytotic route, analogous to that in epithelia, exists in neurons, where it transports proteins from the somatodendritic to the axonal domain. Cultured neurons expressing

the polymeric Ig receptor offer an exptl. system that should be useful for further characterization of this novel neuronal pathway at the mol. and functional level.

L6 ANSWER 35 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:600304 CAPLUS
DOCUMENT NUMBER: 119:200304
TITLE: Protein transport to the **dendritic** plasma membrane of cultured neurons is regulated by rab8p
AUTHOR(S): Huber, Lukas A.; de Hoop, Meltsje J.; Dupree, Paul; Zerial, Marino; Simons, Kai; Dotti, Carlos
CORPORATE SOURCE: Cell Biol. Programme, Eur. Mol. Biol. Lab., Heidelberg, D-69012, Germany
SOURCE: J. Cell Biol. (1993), 123(1), 47-55
CODEN: JCLBA3; ISSN: 0021-9525
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In the companion paper (Huber, L. A.; et al., 1993) the authors reported that the small GTPase rab8p is involved in transport from the TGN to the basolateral plasma membrane in epithelia. In the present work the authors investigated the localization and function of rab8p in polarized hippocampal neurons. By immunofluorescence microscopy the authors found that rab8p localized preferentially in the somatodendritic domain, and was excluded from the axon. Double-labeling immunofluorescence showed that some of the rab8p colocalized in the **dendrites** with the **Semliki Forest** Virus glycoprotein E2 (SFV-E2). An antisense oligonucleotide approach was used to investigate the role of rab8p in **dendritic** transport of newly synthesized viral glycoproteins. Antisense oligonucleotides corresponding to the initiation region of the rab8 coding sequence were added to the cultured neurons for 4 days. This treatment resulted in a significant decrease in cellular levels of rab8p and transport of SFV-E2 from the cell body to the **dendrites** was significantly reduced. However, no effect was obsd. on axonal transport of influenza HA. Thus, rab8p is involved in transport of proteins to the **dendritic** surface in neurons.

L6 ANSWER 36 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:512568 CAPLUS
DOCUMENT NUMBER: 119:112568
TITLE: Expression of heterologous proteins in cultured rat hippocampal neurons using the **Semliki Forest** virus vector
AUTHOR(S): Olkkonen, V. M.; Liljestroem, P.; Garoff, H.; Simons, K.; Dotti, C. G.
CORPORATE SOURCE: Cell Biol. Programme, Eur. Mol. Biol. Lab.,

Heidelberg, 6900, Germany
SOURCE: J. Neurosci. Res. (1993), 35(4), 445-51
CODEN: JNREDK; ISSN: 0360-4012
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The **Semliki Forest** virus expression vector (Liljestroem, P.; Garoff, H., 1991) was tested in cultured rat hippocampal neurons using two MDCK cell membrane-assocd. proteins as reporters: rab8, a small GTPase involved in post-Golgi vesicle transport, and VIP21, an integral membrane protein of caveolae, trans-Golgi network, and post-Golgi vesicles. Expression of the c-myc epitope-tagged proteins was visualized by immunofluorescence microscopy. The proteins were first detected in neurons after 3-4 h infection by the recombinant viruses. The infection efficiency on neurons was high: after 6 h infection at a multiplicity of one, 50-60% of the cells expressed the reporter proteins. The neurons tolerated the infection well .ltoreq.8 h. Their polarized organization was not disturbed, as judged from morphol. and from distribution of the **dendritic** MAP2 and axonal synaptophysin marker proteins. The **Semliki Forest** virus vector thus seems suitable for short-term expression of proteins in cultured neurons.

L6 ANSWER 37 OF 37 CAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER: 1993:405888 CAPLUS
DOCUMENT NUMBER: 119:5888
TITLE: Polarized distribution of the viral glycoproteins of vesicular stomatitis, fowl plague and **Semliki Forest** viruses in hippocampal neurons in culture: a light and electron microscopy study
AUTHOR(S): Dotti, Carlos G.; Kartenbeck, Juergen; Simons, Kai
CORPORATE SOURCE: Cell Biology Program, European Molecular Biology Laboratory, Heidelberg, Germany
SOURCE: Brain Res. (1993), 610(1), 141-7
CODEN: BRREAP; ISSN: 0006-8993
DOCUMENT TYPE: Journal
LANGUAGE: English

AB It has been shown previously using immunofluorescence microscopy that upon infection of polarized hippocampal cells in culture with vesicular stomatitis virus (VSV) and fowl plague virus (FPV) the VSV glycoprotein is delivered to the plasma membrane of the **dendrites** and of the cell body, whereas the FPV hemagglutinin is transported to the axonal surface. In this work electron microscopy of infected rat hippocampal neurons showed that VSV progeny budded from the plasma membrane of the **dendrites** and the cell body. The location of the budding virions corresponded

to the distribution of the VSV glycoprotein which was detected over the somatodendritic plasma membrane by immunoelectron microscopy. In contrast, no FPV formation was seen in the infected neurons, although the FPV hemagglutinin was localized to the axonal surface by immunoelectron microscopy. In **Semliki Forest** virus (SFV)-infected hippocampal cells, the viral glycoproteins were exclusively present in the **dendrites** and cell body but not in axons.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:40:47 ON 19 SEP 2001)

L7 136 S L6
L8 13 S L7 AND ("E2" OR RESIDUE(5A)160)
L9 45 S L7 AND RECOMBINAN?
L10 57 S L8 OR L9
L11 33 DUP REM L10 (24 DUPLICATES REMOVED)

L11 ANSWER 1 OF 33 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2001-316326 [33] WPIDS
CROSS REFERENCE: 2001-308587 [31]
DOC. NO. CPI: C2001-097446
TITLE: New isolated and purified gp100 useful for the prophylactic treatment of cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): BARBER, B; BERINSTEIN, N; MOINGEON, P; TARTAGLIA, J; TINE, J A
PATENT ASSIGNEE(S): (AVET) AVENTIS PASTEUR LTD
COUNTRY COUNT: 94
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001030847	A1	20010503	(200133)*	EN	89

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001010137 A 20010508 (200149)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001030847	A1	WO 2000-CA1254	20001020
AU 2001010137	A	AU 2001-10137	20001020

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001010137 A	Based on	WO 200130847

PRIORITY APPLN. INFO: US 2000-223325 20000807; US 1999-160879 19991022

AN 2001-316326 [33] WPIDS

CR 2001-308587 [31]

AB WO 200130847 A UPAB: 20010831

NOVELTY - An isolated and purified modified gp100 molecule (N1) capable of modulating an immune response in an animal is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for:

(1) a cell comprising (N1) where the cell expresses a polypeptide encoded by the nucleic acid;

(2) a **recombinant** virus comprising a virus into which (N1) has been inserted which encodes for a polypeptide, where the virus causes the expression of the polypeptide in an infected cell;

(3) a **recombinant** virus into which (N1) has been inserted which encodes for a polypeptide where cells infected with the virus are capable of eliciting an immune response directly against a member selected from:

(a) the polypeptide;

(b) a fragment of the polypeptide;

(c) a cell expressing the polypeptide or a fragment of it; or

(d) cells binding the protein or fragment of it;

(4) an isolated protein encoded by (N1);

(5) an isolated protein having the activity of a modified gp100 protein;

(6) a protein having a sequence of 661 amino acids described in the specification;

(7) modulating an animal's immune system comprising administering an effective amount of a gp100 or gp100 protein which has been modified;

(8) modulating an animal's immune system comprising administering to an animal in need of it, an effective amount of a vector, into which gp100 which has been modified is inserted;

(9) prophylactic treatment of cancer comprising administering to an animal an effective amount of a modified gp100 or immunogenic fragment of it, or a nucleic acid sequence encoding a modified gp100 or immunogenic fragment of it;

(10) a melanoma vaccine comprising a nucleic acid sequence encoding a modified gp100;

(11) a modified gp100 protein sequence which is modified to enhance its binding to MHC molecules;

(12) a vaccine comprising a modified gp100 nucleic acid

sequence or its corresponding protein or protein fragment capable of eliciting the production of antibodies in a animal to corresponding antigens;

(13) a vaccine comprising a modified gp100 nucleic acid sequence or its corresponding protein or protein fragment capable of eliciting a cellular immune response; and

(14) an immunogenic composition containing a vaccine vector encoding for a modified gp100 molecule.

ACTIVITY - Cytostatic.

MECHANISM OF ACTION - Vaccine; Gene therapy.

USE - Nucleic acids and proteins of the invention are useful as vaccines for prophylactic treatment of cancer (claimed).

Dwg.0/12

L11 ANSWER 2 OF 33 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2001-235115 [24] WPIDS

DOC. NO. CPI: C2001-070478

TITLE: Introducing nucleic acid into cell, useful e.g. in gene therapy of tumors, using **alphavirus** vector and vector-specific antibody to enhance infection.

DERWENT CLASS: B04 C06 D16

INVENTOR(S): JOHNSTON, R E; MACDONALD, G H

PATENT ASSIGNEE(S): (UYNC-N) UNIV NORTH CAROLINA

COUNTRY COUNT: 94

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2001016343	A1	20010308	(200124)*	EN	66

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000074718 A 20010326 (200137)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2001016343	A1	WO 2000-US23845	20000830
AU 2000074718	A	AU 2000-74718	20000830

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2000074718 A	Based on		WO 200116343

PRIORITY APPLN. INFO: US 2000-177435 20000121; US 1999-151718 19990831

AN 2001-235115 [24] WPIDS

AB WO 200116343 A UPAB: 20010502

NOVELTY - Introducing and expressing a nucleic acid (I) in a cell by contacting the cell with an **alphavirus** vector (A) containing heterologous (I), and an antibody (Ab) that binds specifically to (A), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) delivering (I) to a subject by administering:

(a) (A) and Ab;

(b) (A) only if the subject already contains Ab; or

(c) a cell previously contacted with (A) and Ab;

(2) generating an immune response, by administering:

(a) an (A) in which (I) encodes an immunogen and Ab;

(b) (A) only if the subject already contains Ab; or

(c) a cell previously contacted with (A) and Ab; and

(3) pharmaceutical formulation comprising a complex of (A) and Ab in a carrier.

ACTIVITY - Cytostatic; antiviral; antibacterial; antiprotozoal; antiparasitic.

No biological data is given.

MECHANISM OF ACTION - Induction of specific immune responses, both humoral and cellular; gene therapy; low concentrations of Ab form, with (A), complexes that interact with Fc or complement receptors on cells, preferably APCs, resulting in increased infectivity.

USE - The method is used to express (I) in humans or other animals (mammals and birds). (I) encodes an antigen from a tumor or infectious agent, particularly a latent or chronic agent, including bacterium, virus, protozoan or parasite. (I) may encode a therapeutic protein, for treating a wide range of genetic or acquired disorders, a protein that confers resistance to anticancer agents or an immunostimulant. Alternatively, (I) encodes a therapeutic RNA. (All claimed). (I) can be used to treat infectious diseases, or tumors. The method can be used for transient or stable expression of (I) in cultured cells, or for preparation of transgenic animals. Antibodies raised against the new immunogenic compositions can be used for passive immunization or for diagnosis or histological applications.

ADVANTAGE - Ab increases the infectivity of (A) for particular cell types and may target (A) to antigen-presenting cells, resulting in an increased immune response, i.e. even weak antigens that fail

when used in conventional compositions may be used successfully. When formulated with Ab, (A) induces a stronger immune response than the corresponding infectious organism itself. With **alphaviruses**, antibody-dependent enhancement is not associated with significant pathology.
Dwg.0/8

L11 ANSWER 3 OF 33 MEDLINE
ACCESSION NUMBER: 2001231630 MEDLINE
DOCUMENT NUMBER: 21221117 PubMed ID: 11296257
TITLE: Activation-dependent changes in receptor distribution and **dendritic** morphology in hippocampal neurons expressing P2X2-green fluorescent protein receptors.
AUTHOR: Khakh B S; Smith W B; Chiu C S; Ju D; Davidson N; Lester H A
CORPORATE SOURCE: Division of Biology, 156-29, California Institute of Technology, Pasadena, CA 91125, USA..
bsk@mrc-lmb.com.ac.uk
CONTRACT NUMBER: MH49176 (NIMH)
NS-11756 (NINDS)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (2001 Apr 24) 98 (9) 5288-93.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200105
ENTRY DATE: Entered STN: 20010529
Last Updated on STN: 20010529
Entered Medline: 20010521

AB ATP-gated P2X(2) receptors are widely expressed in neurons, but the cellular effects of receptor activation are unclear. We engineered functional green fluorescent protein (GFP)-tagged P2X(2) receptors and expressed them in embryonic hippocampal neurons, and report an approach to determining functional and total receptor pool sizes in living cells. ATP application to **dendrites** caused receptor redistribution and the formation of varicose hot spots of higher P2X(2)-GFP receptor density. Redistribution in **dendrites** was accompanied by an activation-dependent enhancement of the ATP-evoked current. Substate-specific mutant T18A P2X(2)-GFP receptors showed no redistribution or activation-dependent enhancement of the ATP-evoked current. Thus fluorescent P2X(2)-GFP receptors function normally, can be quantified, and reveal the dynamics of P2X(2) receptor distribution on the seconds time scale.

L11 ANSWER 4 OF 33 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2001:391128 SCISEARCH
THE GENUINE ARTICLE: 430EG
TITLE: **Sindbis** viral-mediated expression of Ca2+-permeable AMPA receptors at hippocampal CA1 synapses and induction of NMDA receptor-independent long-term potentiation
AUTHOR: Okada T; Yamada N; Kakegawa W; Tsuzuki K; Kawamura M; Nawa H; Iino M; Ozawa S (Reprint)
CORPORATE SOURCE: Gunma Univ, Sch Med, Dept Physiol, 3-39-22 Showa Machi, Gunma 3718511, Japan (Reprint); Gunma Univ, Sch Med, Dept Physiol, Gunma 3718511, Japan; Japan Sci & Technol Corp, CREST, Kawaguchi, Saitama 3320012, Japan; Niigata Univ, Brain Res Inst, Dept Mol Neurobiol, Niigata 9518585, Japan
COUNTRY OF AUTHOR: Japan
SOURCE: EUROPEAN JOURNAL OF NEUROSCIENCE, (APR 2001) Vol. 13, No. 8, pp. 1635-1643.
Publisher: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND.
ISSN: 0953-816X.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 34

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Gene manipulation in order to artificially express a particular gene in neurons in the central nervous system is a powerful tool for the analysis of brain function. **Sindbis** viral vectors have been developed to express high levels of foreign genes in postmitotic brain neurons with little transfection of glial cells. In this study, we expressed the gene encoding the unedited GluR2 (GluR-B) subunit of the AMPA-type glutamate receptor that forms inwardly rectifying and Ca2+-permeable channels, in rat CA1 hippocampal neurons in slice cultures using **Sindbis** viral vectors. The pyramidal cell layer of the CA1 region was injected with **recombinant Sindbis** viruses encoding both enhanced green fluorescent protein (GFP) and unedited GluR2. The GFP fluorescence from CA1 neurons could be detected as early as 6 h and reached a maximal level about 48 h postinfection. The inwardly rectifying and Ca2+-permeable AMPA receptors were expressed in most CA1 pyramidal cells expressing GFP. These AMPA receptors expressed by gene transfer were involved in fast excitatory neurotransmission elicited by electrical stimulation of the Schaffer collaterals in the stratum radiatum. Tetanic stimulation of Schaffer collaterals induced NMDA receptor-independent, long-term potentiation due to Ca2+ influx through the newly expressed AMPA receptors in the area densely stained with GFP. Thus, the combined use of **Sindbis** viral vectors with the GFP reporter allowed physiological

examination of the roles of a specific gene product in synaptic function in well-characterized brain neurons.

L11 ANSWER 5 OF 33 MEDLINE DUPLICATE 1
ACCESSION NUMBER: 2001450312 IN-PROCESS
DOCUMENT NUMBER: 21387414 PubMed ID: 11495971
TITLE: Abundant gfp expression and ltp in hippocampal acute slices by in vivo injection of **sindbis** virus.
AUTHOR: D'Apuzzo M; Mandolesi G; Reis G; Schuman E M
CORPORATE SOURCE: California Institute of Technology, Pasadena, California 91125.
SOURCE: JOURNAL OF NEUROPHYSIOLOGY, (2001 Aug) 86 (2) 1037-42.
Journal code: JC7; 0375404. ISSN: 0022-3077.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 20010813
Last Updated on STN: 20010813

AB Virus-mediated gene transfer into neurons is a powerful tool for the analysis of neuronal structure and function. **Recombinant sindbis** virus has been previously used to study protein function in hippocampal neuron cultures as well as in hippocampal organotypic slice cultures. Nevertheless, some concern still exists about the physiological relevance of these cultured preparations. Acute hippocampal slices are a widely used preparation for the study of synaptic transmission, but currently **recombinant** gene delivery is usually achieved only through time-consuming transgenic techniques. In this study, we show that a subregion of the CA1 area in acute hippocampal slices can be specifically altered to express a gene of interest. A **sindbis** virus vector carrying an enhanced green fluorescent protein (EGFP) reporter was injected in vivo into the hippocampus of adult rats. After 18 h, rats were killed, and acute hippocampal slices, infected in the CA1 field, were analyzed morphologically and electrophysiologically. Infected slices showed healthy and stable electrophysiological responses as well as long-term potentiation. In addition, infected pyramidal cells were readily recognized in living slices by two-photon imaging. Specifically, the introduction of an EGFP-Actin fusion protein greatly enhanced the detection of fine processes and **dendritic** spines. We propose this technique as an efficient tool for studying gene function in adult hippocampal neurons.

L11 ANSWER 6 OF 33 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001290084 EMBASE
TITLE: Gene delivery of vaccines for infectious disease.

AUTHOR: Clark K.R.; Johnson P.R.
CORPORATE SOURCE: P.R. Johnson, Children's Research Institute, Department of Pediatrics, The Ohio State University, Columbus, OH 43205, United States. johnsonp@pediatrics.ohio-state.edu
SOURCE: Current Opinion in Molecular Therapeutics, (2001) 3/4 (375-384).
Refs: 65
ISSN: 1464-8431 CODEN: CUOTFO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Genetic immunization is the process of delivering and expressing a gene (or therapeutic nucleic acid) encoding a pathogen-derived antigen into target host cells to elicit a protective humoral or cell-mediated immune response. Gene delivery methods to achieve this goal have expanded rapidly, and currently employ a variety of oligonucleotides, synthetic polypeptides, **recombinant** vectors and even edible plants, all of which have been shown to be capable of inducing protective immunity in experimental animal models. This review highlights recent progress in several gene delivery systems (both non-viral and viral methods) using novel in vivo approaches to engender effective host immune responses against the introduced antigen.

L11 ANSWER 7 OF 33 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2001081556 EMBASE
TITLE: Web alert: Molecular vaccines for disease prevention and therapy.
AUTHOR: Jones D.
CORPORATE SOURCE: D. Jones, Current Drugs Ltd, Middlesex House, 34-42 Cleveland St., London W1T 4LB, United Kingdom. daniel.jones@current-drugs.com
SOURCE: Current Opinion in Molecular Therapeutics, (2001) 3/1 (11-12).
ISSN: 1464-8431 CODEN: CUOTFO
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
016 Cancer
026 Immunology, Serology and Transplantation

037 Drug Literature Index
LANGUAGE: English

L11 ANSWER 8 OF 33 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-619231 [59] WPIDS
DOC. NO. CPI: C2000-185549
TITLE: New **alphavirus** that infects human **dendritic** cells for use in generating an immune response to pathogenic agents such as bacteria, viruses, fungi, parasites and cancer and for biological assays.
DERWENT CLASS: B04 D16
INVENTOR(S): BARNETT, S; DRIVER, D A; DUBENSKY, T W; FROLOV, I; GARDNER, J P; OTTEN, G; POLO, J M
PATENT ASSIGNEE(S): (CHIR) CHIRON CORP
COUNTRY COUNT: 92
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000061772	A2	20001019	(200059)*	EN	83
AU 2000043660	A	20001114	(200108)		

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000061772	A2	WO 2000-US10722	20000414
AU 2000043660	A	AU 2000-43660	20000414

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000043660	A Based on	WO 200061772

PRIORITY APPLN. INFO: US 2000-191363 20000322; US 1999-129498 19990414; US 1999-148086 19990809
AN 2000-619231 [59] WPIDS
AB WO 200061772 A UPAB: 20001117
NOVELTY - An isolated **alphavirus** (AV) which infects human

dendritic cells and is not of American Type Culture Collection (ATCC) number **VR-2526**, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated AV which infects non-human **dendritic** cells and is not a **Venezuelan equine** encephalitis **virus** or ATCC **VR-2526**;

(2) an isolated nucleic acid comprising a nucleic acid which encodes AV;

(3) an isolated nucleic acid comprising a nucleic acid that encodes an AV, having a sequence of 11703 nucleotides, given in the specification;

(4) an AV structural protein cassette, comprising a promoter operably linked to a nucleic acid sequence encoding AV structural proteins (sP) from the new AV;

(5) an AV packaging cell, comprising a host cell and (4);

(6) an AV producer cell, comprising (5) and an **alphavirus** RNA vector replicon, an **alphavirus** vector construct, or a eukaryotic layered vector initiation system;

(7) a **recombinant** AV particle, comprising a particle produced from a cell line of (6);

(8) a **recombinant** AV particle, comprising a particle produced from a cell line of (5);

(9) a **recombinant** AV particle which infects human **dendritic** cells and that is not derived from ATCC **VR -2526**;

(10) a **recombinant** AV particle which infects non-human **dendritic** cells and that is not derived from a **Venezuelan equine** encephalitis **virus** or ATCC **VR-2526**;

(11) introducing a heterologous nucleotide sequence into cells, comprising infecting the cells with (7), (8), (9) or (10);

(12) an AV vector construct comprising:

(a) a 5' promoter that initiates synthesis of viral RNA in vitro from cDNA;

(b) a 5' sequence that initiates transcription of AV RNA;

(c) a nucleic acid molecule that operably encodes all 4 AV nsP's;

(d) an AV RNA polymerase recognition sequence; and

(e) a 3' polyadenylate tract, where the nucleic acid sequence that operably encodes all 4 AV nonstructural proteins (nsP) contains a mutation in at least one nsP that is a mutation in nsP1 residues 346, 441, 473, nsP2 residues 438, 622, 634, 715, nsP3 residues, 417, 456, 505, and nsP4 residue 266, as compared to wild-type;

(13) a eukaryotic layered vector initiation system, comprising a 5' promoter capable of initiating in vivo the 5' synthesis of AV RNA from cDNA, a sequence which initiates transcription of AV RNA following the 5' promoter, a nucleic acid which operably encodes all

4 AV nonstructural proteins, an AV RNA polymerase recognition sequence, and a 3' polyadenylate tract, where the nucleic acid sequence which operably encodes all 4 AV nsP's contains a mutation in at least one nsP that is a mutation in nsP1 residues 346, 441, 473, nsP2 residues 438, 622, 634, 715, nsP3 residues, 417, 456, 505, and nsP4 residue 266, as compared to wild-type; and

(14) an AV RNA vector replicon capable of translation in a eukaryotic system, comprising a 5' sequence which initiates transcription of AV RNA, a nucleic acid molecule which operably encodes all 4 AV nsP's, an AV RNA polymerase recognition sequence, and a 3' polyadenylate tract, where the nucleic acid sequence which operably encodes all 4 AV nsP's contains a mutation in at least one nsP that is a mutation in nsP1 residues 346, 441, 473, nsP2 residues 438, 622, 634, 715, nsP3 residues, 417, 456, 505, and nsP4 residue 266, as compared to wild-type.

ACTIVITY - Immunostimulatory; cytostatic; virucide; fungicide; antibacterial; antiparasitic. No suitable biological data is given.

MECHANISM OF ACTION - Vaccine.

USE - The AV's are used to infect **dendritic** cells, preferably human cells (claimed). A heterologous sequence can be introduced and expressed in human macrophages or antigen presenting cells in vivo and in vitro, for use in biological assays. The AV-based vector systems are used to generate an immune response to cancer or a pathogenic agent, such as, bacteria, fungi, parasites or viruses.

ADVANTAGE - The AV can be used to infect human **dendritic** cells, macrophages or antigen presenting cells that previously could not be infected using an AV or AV variant. The AV vectors are targeted directly to antigen presenting cells.

Dwg.0/12

L11 ANSWER 9 OF 33 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD

ACCESSION NUMBER: 2000-452400 [39] WPIDS

CROSS REFERENCE: 2000-452401 [39]; 2000-465745 [39]

DOC. NO. CPI: C2000-137949

TITLE: Expression cassettes encoding the human immunodeficiency virus (HIV) Gag-containing polypeptide useful for vaccinating against HIV infections and acquired immunodeficiency syndrome (AIDS).

DERWENT CLASS: B04 C06 D16

INVENTOR(S): BARNETT, S; GREER, C; HARTOG, K; LIAN, Y; LIU, H; SELBY, M; SRIVASTAVA, I; WALKER, C; ZUR MEGEDE, J

PATENT ASSIGNEE(S): (CHIR) CHIRON CORP

COUNTRY COUNT: 89

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

WO 2000039302 A2 20000706 (200039)* EN 390
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
MW NL OA PT SD SE SL SZ TZ UG ZW
W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM
EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ
LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
AU 2000022216 A 20000731 (200050)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000039302 A2		WO 1999-US31245	19991230
AU 2000022216 A		AU 2000-22216	19991230

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2000022216 A	Based on	WO 200039302

PRIORITY APPLN. INFO: US 1999-168471 19991201; US 1998-114495 19981231

AN 2000-452400 [39] WPIDS

CR 2000-452401 [39]; 2000-465745 [39]

AB WO 200039302 A UPAB: 20001010

NOVELTY - Synthetic expression cassettes comprising nucleic acids encoding the human immunodeficiency virus (HIV) Gag-containing polypeptide, are new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the following:

(1) an expression cassette (I) comprising a polynucleotide sequence encoding a protein comprising a human immunodeficiency virus (HIV) Gag polypeptide (the polynucleotide sequence encoding the Gag polypeptide comprises a sequence with at least 90% sequence identity to a defined 60 nucleotide sequence (N1) given in the specification);

(2) a **recombinant** expression system (II) for use in a host cell comprising (I) operably linked to control elements suitable or protein expression in the host;

(3) a cell (III) comprising (II);

(4) a method (IV) for producing polypeptides including HIV Gag polypeptide sequences, comprising incubating (III) under conditions suitable for expression of the polypeptide;

(5) a method (V) for producing virus-like particles (VLPs), comprising incubating (III) under conditions suitable for production

of VLPs; and

(6) a method (VI) for DNA vaccination of a subject, comprising introducing (II) into a subject under conditions suitable for gene expression.

ACTIVITY - Anti-HIV.

MECHANISM OF ACTION - Vaccine.

USE - The expression cassettes may be used for the **recombinant** expression of HIV Gag-polypeptides which may then be used to vaccinate against HIV infection and acquired immunodeficiency syndrome (AIDS).

Dwg.0/82

L11 ANSWER 10 OF 33 WPIDS COPYRIGHT 2001 DERWENT INFORMATION LTD
ACCESSION NUMBER: 2000-431307 [37] WPIDS
DOC. NO. CPI: C2000-131084
TITLE: Novel **recombinant** vector useful as immunogens and vaccines for stimulating and enhancing immunological responses to target cells and antigens expresses multiple co-stimulatory molecules such as B7-1, LFA-3, ICAM-1.
DERWENT CLASS: B04 D16
INVENTOR(S): HODGE, J; PANICALI, D; SCHLOM, J
PATENT ASSIGNEE(S): (THER-N) THERION BIOLOGICS CORP; (USSH) US DEPT HEALTH & HUMAN SERVICES
COUNTRY COUNT: 90
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2000034494	A1	20000615	(200037)*	EN	188

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW

W: AE AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2000016218 A 20000626 (200045)

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000034494	A1	WO 1999-US26866	19991112
AU 2000016218	A	AU 2000-16218	19991112

FILING DETAILS:

PATENT NO	KIND	PATENT NO

AU 2000016218 A Based on WO 200034494

PRIORITY APPLN. INFO: US 1998-111582 19981209
AN 2000-431307 [37] WPIDS
AB WO 200034494 A UPAB: 20000807
NOVELTY - A **recombinant** vector (I), comprising foreign nucleic acid sequences encoding multiple co-stimulatory molecules (CM), or functional portions of them, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a pharmaceutical composition, comprising (I) or a **recombinant** vector comprising a nucleic sequence encoding a target antigen or an immunological epitope, and a carrier;

(2) a host cell (II) infected, transfected or induced with (I);

(3) a **dendritic** cell (III), or its precursor, comprising a foreign nucleic acid sequence encoding multiple CM;

(4) a tumor cell (IV), or its precursor, comprising a foreign nucleic acid sequence encoding multiple CM;

(5) a pharmaceutical composition, comprising (II) and optionally a exogenous source of target antigen or its immunological epitope;

(6) a **recombinant** poxvirus (V) having integrated into its genome a foreign DNA encoding multiple CM which is produced by allowing a plasmid vector comprising the foreign DNA encoding multiple CM to undergo recombination with the parental poxvirus genome to produce **recombinant** poxvirus with the foreign DNA inserted into its genome;

(7) a **recombinant** poxvirus (VI) having integrated into its genome a foreign DNA encoding leukocyte function-associated antigen (LFA)-3, intracellular adhesion molecule (ICAM)-1 and at least one B7 molecule, produced by allowing a vector comprising the DNA to undergo recombination with a parenteral poxvirus genome to produce the **recombinant** virus;

(8) a pharmaceutical composition comprising (V), or (VI), and a carrier;

(9) a host cell (VII) infected with (V) or (VI);

(10) a plasmid vector (VIII) comprising nucleic acid sequences encoding multiple CM or its functional portions;

(11) a plasmid vector (IX) for recombination with a poxvirus designed to produce **recombinant** poxvirus capable of expressing foreign nucleic acid encoding LFA-3, ICAM-1, and at least one B7 molecule, comprising poxviral promoters, the DNA encoding the costimulatory molecules, and DNA sequences flanking the construct of the promoters and DNA, which are homologous to a region of the poxvirus genome into which the construct is to insert;

(12) a kit for use in making (V) of (VI), comprising (VIII) or (IX), and optionally a parental poxvirus; and

(13) making (V), or (VI) which involves allowing (VIII), or (IX) to undergo recombination with a parental poxvirus genome to produce **recombinant** poxvirus with the foreign DNA inserted into its genome and a multiplicity of poxvirus promoters capable of controlling the expression of the foreign DNA.

ACTIVITY - Antitumor; Cytostatic; antibacterial; antiviral; antifungal; antiprotozoan; antiulcer; antiinflammatory; antiparasitic. The cytostatic activity of (I) was tested using mice. A four-gene vaccinia **recombinant** was constructed that contained the human CEA (carcinoembryonic antigen) gene and the B7-1, ICAM-1 (intercellular adhesion molecule-1) and LFA-3 (leukocyte function associated antigen-3) genes, designated rV-CEA/TRICOM. Six to eight-week-old female C57 BL/6 mice C57BL/6 mice transgenic for human CEA (Kass,E et al Cancer Res 59:676-683, 1999) were vaccinated by tail scarification with 107 plaque forming units rV-CEA, rV-CEA/B7-1 or rV-CEA/TRICOM, and spleens were harvested 22 days later. Lymphoproliferative activity of splenocytes was analyzed. Splenic T-cells of mice vaccinated with rV-TRICOM showed higher levels of CEA-specific stimulation compared with T-cells obtained from mice vaccinated with rV-CEA.

MECHANISM OF ACTION - Vaccine; gene therapy.

USE - (I) is useful for enhancing an cell-mediated or humoral immune response in an individual. (V) is used for enhancing an antigen specific T-cell response in an individual to a target antigen. (II) is used in immunotherapy for treating or preventing diseases caused by viruses, bacteria, protozoans, parasites, premalignant cells and tumor cells. (III) or (IV) are also used in enhancing an immune response in an individual. (I) is used for making a progenitor DC, or DC derived from bone marrow or peripheral blood mononuclear cells that overexpresses multiple CM which involves providing a cell with (I) for a sufficient period of time to cause of overexpression of multiple CM. (II) is also used for assessing the efficacy of a vaccine against target antigen. (II) is used for screening novel immunogenic peptides from a combinatorial peptide library source which involves, pulsing APC infected with (I) with the peptides to form peptide-pulsed APC, and measuring lymphoid immunoreactivity in the presence of peptide-pulsed APC. An enhanced immunoreactivity is indicative of an immunogenic peptide-pulsed APC. (All claimed). (I) is useful as an immunogen and vaccine against pathogenic microorganisms and cancer and as diagnostic agents. The **recombinant** vector can be used to treat or prevent preneoplastic or hyperplastic states such as colon polyps, Crohn's disease, ulcerative colitis and breast lesions.

ADVANTAGE - The enhancement of the immunological response using the **recombinant** vectors expressing multiple costimulatory molecules is synergistic compared to the use of a single costimulatory molecule, or the use of two costimulatory molecules in enhancing immunological responses. The magnitude of the immune

response against the target antigen, epitope, or cells expressing target antigen obtained using the **recombinant** vector is significantly greater than that achieved using systems employing a single or a double costimulatory molecule (claimed).

DESCRIPTION OF DRAWING(S) - The figure shows the genomic structure of pT5032 comprising nucleic acid sequences encoding murine LFA-3 (leukocyte function associated antigen-3), ICAM-1 (intercellular adhesion molecule-1), B7.1, flanked by portions of the Honda M region of the vaccinia genome.

Dwg.1/54

L11 ANSWER 11 OF 33 MEDLINE

ACCESSION NUMBER: 2001069343 MEDLINE

DOCUMENT NUMBER: 20519611 PubMed ID: 10924501

TITLE: The metabotropic GABAB receptor directly interacts with the activating transcription factor 4.

AUTHOR: Nehring R B; Horikawa H P; El Far O; Kneussel M; Brandstatter J H; Stamm S; Wischmeyer E; Betz H; Karschin A

CORPORATE SOURCE: Department of Molecular Neurobiology of Signal Transduction, Max Planck Institute for Biophysical Chemistry, 37070 Gottingen, Germany.

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Nov 10) 275 (45) 35185-91.
Journal code: HIV. ISSN: 0021-9258.

PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200101

ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010104

AB G protein-coupled receptors regulate gene expression by cellular signaling cascades that target transcription factors and their recognition by specific DNA sequences. In the central nervous system, heteromeric metabotropic gamma-aminobutyric acid type B (GABA(B)) receptors through adenylyl cyclase regulate cAMP levels, which may control transcription factor binding to the cAMP response element. Using yeast-two hybrid screens of rat brain libraries, we now demonstrate that GABA(B) receptors are engaged in a direct and specific interaction with the activating transcription factor 4 (ATF-4), a member of the cAMP response element-binding protein /ATF family. As confirmed by pull-down assays, ATF-4 associates via its conserved basic leucine zipper domain with the C termini of both GABA(B) receptor (GABA(B)R) 1 and GABA(B)R2 at a site which serves to assemble these receptor subunits in heterodimeric complexes. Confocal fluorescence microscopy shows that GABA(B)R and ATF-4 are

strongly coclustered in the soma and at the **dendritic** membrane surface of both cultured hippocampal neurons as well as retinal amacrine cells in vivo. In oocyte coexpression assays short term signaling of GABA(B)Rs via G proteins was only marginally affected by the presence of the transcription factor, but ATF-4 was moderately stimulated in response to receptor activation in in vivo reporter assays. Thus, inhibitory metabotropic GABA(B)Rs may regulate activity-dependent gene expression via a direct interaction with ATF-4.

L11 ANSWER 12 OF 33 MEDLINE DUPLICATE 2
ACCESSION NUMBER: 2001083046 MEDLINE
DOCUMENT NUMBER: 20541985 PubMed ID: 11090185
TITLE: Infection of human **dendritic** cells by a **sindbis** virus replicon vector is determined by a single amino acid substitution in the **E2** glycoprotein.
AUTHOR: Gardner J P; Frolov I; Perri S; Ji Y; MacKichan M L; zur Megede J; Chen M; Belli B A; Driver D A; Sherrill S; Greer C E; Otten G R; Barnett S W; Liu M A; Dubensky T W; Polo J M
CORPORATE SOURCE: Vaccines & Gene Therapy, Chiron Corporation, Emeryville, California 94608, USA.
SOURCE: JOURNAL OF VIROLOGY, (2000 Dec) 74 (24) 11849-57. Journal code: KCV. ISSN: 0022-538X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010111

AB The ability to target antigen-presenting cells with vectors encoding desired antigens holds the promise of potent prophylactic and therapeutic vaccines for infectious diseases and cancer. Toward this goal, we derived variants of the prototype **alphavirus**, **Sindbis** virus (SIN), with differential abilities to infect human **dendritic** cells. Cloning and sequencing of the SIN variant genomes revealed that the genetic determinant for human **dendritic** cell (**DC**) tropism mapped to a single amino acid substitution at **residue 160** of the envelope glycoprotein **E2**. Packaging of SIN replicon vectors with the **E2** glycoprotein from a **DC** -tropic variant conferred a similar ability to efficiently infect immature human **DC**, whereupon those **DC** were observed to undergo rapid activation and maturation. The SIN replicon particles infected skin-resident mouse **DC** in

vivo, which subsequently migrated to the draining lymph nodes and upregulated cell surface expression of major histocompatibility complex and costimulatory molecules. Furthermore, SIN replicon particles encoding human immunodeficiency virus type 1 p55(Gag) elicited robust Gag-specific T-cell responses in vitro and in vivo, demonstrating that infected **DC** maintained their ability to process and present replicon-encoded antigen. Interestingly, human and mouse **DC** were differentially infected by selected SIN variants, suggesting differences in receptor expression between human and murine **DC**. Taken together, these data illustrate the tremendous potential of using a directed approach in generating **alphavirus** vaccine vectors that target and activate antigen-presenting cells, resulting in robust antigen-specific immune responses.

L11 ANSWER 13 OF 33 MEDLINE DUPLICATE 3
ACCESSION NUMBER: 2000129590 MEDLINE
DOCUMENT NUMBER: 20129590 PubMed ID: 10666209
TITLE: Stimulation of cytotoxic T cells against idiotype immunoglobulin of malignant lymphoma with protein-pulsed or idiotype-transduced **dendritic** cells.
AUTHOR: Osterroth F; Garbe A; Fisch P; Veelken H
CORPORATE SOURCE: Departments of Hematology/Oncology and Pathology, Freiburg University Medical Center, Freiburg, Germany.
SOURCE: BLOOD, (2000 Feb 15) 95 (4) 1342-9.
Journal code: A8G; 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000314

AB Because of their hypervariable regions and somatic mutations, the antigen receptor molecules of lymphomas (idiotypes) are tumor-specific antigens and attractive targets for antilymphoma immunotherapy. For the optimal induction of human idiotype-specific cytotoxic T cells (CTL), idiotype was presented to CD8(+) peripheral blood mononuclear cells by monocyte-derived autologous **dendritic** cells (**DC**) after the endocytosis of idiotype protein or by idiotype-expressing **DC**. **Recombinant** idiotype was obtained as a functionally folded Fab fragment by periplasmic expression in Escherichia coli. Idiotype-expressing **DC** were generated by transduction with **recombinant Semliki forest** virus vectors

encompassing heavy- or light-chain idiotype genes. Autologous lymphoblastoid cell lines stably transfected with Epstein-Barr virus-based idiotype expression vectors were used as target cells to detect idiotype-specific lysis. CTL stimulated with idiotype-loaded **DC** showed strong specific, CD8-mediated, and major histocompatibility complex (MHC) class I-restricted cytotoxicity against autologous heavy- and light-chain idiotype. In contrast, stimulation with idiotype-transduced **DC** resulted in only moderate natural killer cell activity. These data confirm the existence of idiotype-specific CTL in patients with lymphoma, define a "good manufacturing practice"-compatible protocol for the generation of these cells without the requirement of viable lymphoma cells, and favor the processing of exogenous antigen over **DC** transduction for the induction of MHC I-restricted CTL against idiotypes with unknown antigenicity. (Blood. 2000;95:1342-1349)

L11 ANSWER 14 OF 33 MEDLINE DUPLICATE 4
ACCESSION NUMBER: 2000091347 MEDLINE
DOCUMENT NUMBER: 20091347 PubMed ID: 10623754
TITLE: Role of **dendritic** cell targeting in **Venezuelan equine** encephalitis **virus** pathogenesis.
AUTHOR: MacDonald G H; Johnston R E
CORPORATE SOURCE: Department of Microbiology and Immunology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, North Carolina 27599-7290, USA.. gmacd@med.unc.edu
CONTRACT NUMBER: A122186 (NIAID)
F32-AI09778 (NINDS)
NS26681
SOURCE: JOURNAL OF VIROLOGY, (2000 Jan) 74 (2) 914-22.
Journal code: KCV; 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000218
Last Updated on STN: 20000218
Entered Medline: 20000208

AB The initial steps of **Venezuelan equine** encephalitis **virus** (VEE) spread from inoculation in the skin to the draining lymph node have been characterized. By using green fluorescent protein and immunocytochemistry, **dendritic** cells in the draining lymph node were determined to be the primary target of VEE infection in the first 48 h following inoculation. VEE viral replicon particles, which can undergo only one round of infection, identified Langerhans cells to be the initial set of

cells infected by VEE directly following inoculation. These cells are resident **dendritic** cells in the skin, which migrate to the draining lymph node following activation. A point mutation in the **E2** glycoprotein gene of VEE that renders the virus avirulent and compromises its ability to spread beyond the draining lymph blocked the appearance of virally infected **dendritic** cells in the lymph node in vivo. A second-site suppressor mutation that restores viral spread to lymphoid tissues and partially restore virulence likewise restored the ability of VEE to infect **dendritic** cells in vivo.

L11 ANSWER 15 OF 33 MEDLINE
ACCESSION NUMBER: 2001110759 MEDLINE
DOCUMENT NUMBER: 20565030 PubMed ID: 11112802
TITLE: Imaging high-resolution structure of GFP-expressing neurons in neocortex in vivo.
AUTHOR: Chen B E; Lendvai B; Nimchinsky E A; Burbach B; Fox K; Svoboda K
CORPORATE SOURCE: Howard Hughes Medical Institute, Cold Spring Harbor Laboratory, Cold Spring Harbor, New York 11724, USA.
SOURCE: LEARNING AND MEMORY, (2000 Nov-Dec) 7 (6) 433-41. Journal code: DAB. ISSN: 1072-0502.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010202

AB To detect subtle changes in neuronal morphology in response to changes in experience, one must image neurons at high resolution in vivo over time scales of minutes to days. We accomplished this by infecting postmitotic neurons in rat and mouse barrel cortex with a **Sindbis** virus carrying the gene for enhanced green fluorescent protein. Visualized with 2-photon excitation laser scanning microscopy, infected neurons showed bright fluorescence that was distributed homogeneously throughout the cell, including axonal and **dendritic** arbors. Single **dendritic** spines could routinely be resolved and their morphological dynamics visualized. Viral infection and imaging were achieved throughout postnatal development up to early adulthood (P 8-30), although the viral efficiency of infection decreased with age. This relatively noninvasive method for fluorescent labeling and imaging of neurons allows the study of morphological dynamics of neocortical neurons and their circuits in vivo.

L11 ANSWER 16 OF 33 MEDLINE

ACCESSION NUMBER: 2000454443 MEDLINE
DOCUMENT NUMBER: 20439484 PubMed ID: 10985351
TITLE: Mutagenesis reveals a role for ABP/GRIP binding to GluR2 in synaptic surface accumulation of the AMPA receptor.
AUTHOR: Osten P; Khatri L; Perez J L; Kohr G; Giese G; Daly C; Schulz T W; Wensky A; Lee L M; Ziff E B
CORPORATE SOURCE: Max-Planck Institute for Medical Research, Department of Molecular Neurobiology, Heidelberg, Germany.. posten@mpimf-heidelberg.mpg.de
CONTRACT NUMBER: AG13620 (NIA)
SOURCE: NEURON, (2000 Aug) 27 (2) 313-25.
Journal code: AN8; 8809320. ISSN: 0896-6273.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20001005
Last Updated on STN: 20001005
Entered Medline: 20000926

AB We studied the role of PDZ proteins GRIP, ABP, and PICK1 in GluR2 AMPA receptor trafficking. An epitope-tagged MycGluR2 subunit, when expressed in hippocampal cultured neurons, was specifically targeted to the synaptic surface. With the mutant MycGluR2delta1-10, which lacks the PDZ binding site, the overall **dendritic** intracellular transport and the synaptic surface targeting were not affected. However, over time, Myc-GluR2delta1-10 accumulated at synapses significantly less than MycGluR2. Notably, a single residue substitution, S880A, which blocks binding to ABP/GRIP but not to PICK1, reduced synaptic accumulation to the same extent as the PDZ site truncation. We conclude that the association of GluR2 with ABP and/or GRIP but not PICK1 is essential for maintaining the synaptic surface accumulation of the receptor, possibly by limiting its endocytotic rate..

L11 ANSWER 17 OF 33 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 2000:737596 SCISEARCH
THE GENUINE ARTICLE: 357CC
TITLE: **Recombinant** viruses as a tool for therapeutic vaccination against human cancers
AUTHOR: Bonnet M C; Tartaglia J; Verdier F; Kourilsky P; Lindberg A; Klein M; Moingeon P (Reprint)
CORPORATE SOURCE: AVENTIS PASTEUR, CAMPUS MERIEUX, 1541 AVE MARCEL MERIEUX, F-69280 MARCY LETOILE, FRANCE (Reprint); AVENTIS PASTEUR, F-69280 MARCY LETOILE, FRANCE; AVENTIS PASTEUR, N YORK, ON, CANADA; INST PASTEUR, PARIS, FRANCE

COUNTRY OF AUTHOR: FRANCE; CANADA
SOURCE: IMMUNOLOGY LETTERS, (15 SEP 2000) Vol. 74, No. 1, Sp. iss. SI, pp. 11-25.
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
ISSN: 0165-2478.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 105

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Viral vectors can be used to express a variety of genes in vivo, that encode tumor associated antigens, cytokines, or accessory molecules. For vaccination pur poses, the ideal viral vector should be safe and enable efficient presentation of expressed antigens to the immune system. It should also exhibit low intrinsic immunogenicity to allow for its re-administration in order to boost relevant specific immune responses. Furthermore, the vector system must meet criteria that enable its industrialization. The characteristics of the most promising viral vectors, including retroviruses, poxviruses, adenoviruses, adeno-associated viruses, herpes simplex viruses, and **alphaviruses**, will be reviewed in this communication. Such **recombinant** viruses have been successfully used in animal models as therapeutic cancer vaccines. Based on these encouraging results, a series of clinical studies, reviewed herein, have been undertaken. Human clinical trials, have as of today, allowed investigators to establish that **recombinant** viruses can be safely used in cancer patients, and that such **recombinants** call break immune tolerance against tumor-associated antigens. These promising results are now leading to improved immunization protocols associating **recombinant** viruses with alternate antigen-presentation platforms (prime-boost regimens), in order to elicit broad tumor-specific immune responses (humoral and cellular) against multiple target antigens. (C) 2000 Elsevier Science B.V. All rights reserved.

L11 ANSWER 18 OF 33 BIOSIS COPYRIGHT 2001 BIOSIS

ACCESSION NUMBER: 2001:88317 BIOSIS
DOCUMENT NUMBER: PREV200100088317
TITLE: Viral gene transfer into neurons from hippocampal slices: comparison of **Semliki Forest** virus, adeno-associated virus, and measles virus.
AUTHOR(S): Ehrengruber, M. U. (1); Hennou, S.; Lundstrom, K.; Bueeler, H.; Naim, H. Y.; Gaehwiler, B. H.
CORPORATE SOURCE: (1) Univ Zurich, Zurich Switzerland
SOURCE: Society for Neuroscience Abstracts, (2000) Vol. 26,

No. 1-2, pp. Abstract No.-329.1. print.
Meeting Info.: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000 Society for Neuroscience
. ISSN: 0190-5295.
DOCUMENT TYPE: Conference
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Viral vectors are useful to transfer cDNA into neurons. As diverse viruses have specific biological profiles, the ideal vector choice depends on both the gene and test system under study. We have previously shown that **Semliki Forest** virus (SFV) and **Sindbis** virus, two closely related positive-strand RNA viruses, efficiently infect neurons. In the present study, we characterized distinct vectors in rat hippocampal slice cultures. The following **recombinant** viruses encoding GFP were injected into stratum pyramidale: i) SFV, ii) adeno-associated virus (AAV), a single-strand DNA virus, and iii) measles virus (MV), a negative-strand RNA virus. All viruses efficiently infected pyramidal cells. GFP fluorescence was found in **dendrites** of up to the fourth order and in **dendritic** spines. SFV infected more pyramidal cells (apprx90% of all GFP-positive cells) than either AAV or MV (apprx65%). AAV-mediated GFP expression was more neuron-specific (apprx90%) when a PDGF rather than CMV promoter was used. GFP expression occurred rapidly but was transient for SFV (max. at 1-2 d post-infection, p.i.), increased slowly (from 5 d p.i.) but remained stable with AAV, and was fast (1-2 d p.i.) and persistent with MV. Resting membrane potentials and conductances as well as firing properties of pyramidal cells were normal at 2 and 28 d p.i. for SFV and AAV, respectively. We conclude that SFV is valuable for short-term, AAV for long-term, and MV for both short- and long-term gene transfer into pyramidal cells from hippocampal slices.

ACCESSION NUMBER: 1999-395093 [33] WPIDS
DOC. NO. CPI: C1999-116132
TITLE: Using new **Venezuelan equine encephalitis virus** vectors.
DERWENT CLASS: B04 D16
INVENTOR(S): HIPPENMEYER, P J
PATENT ASSIGNEE(S): (SEAR) SEARLE & CO G D
COUNTRY COUNT: 85
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9930734	A1	19990624	(199933)*	EN	40

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC
MW NL OA PT SD SE SZ UG ZW
W: AL AM AT AU AZ BA BB BG BR BY CA CH CN CU CZ DE DK EE ES FI
GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR
LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
SK SL TJ TM TR TT UA UG US UZ VN YU ZW
AU 9917106 A 19990705 (199948)
EP 1039926 A1 20001004 (200050) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU NL PT SE

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9930734	A1	WO 1998-US25725	19981214
AU 9917106	A	AU 1999-17106	19981214
EP 1039926	A1	EP 1998-961904	19981214
		WO 1998-US25725	19981214

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9917106	A	Based on	WO 9930734
EP 1039926	A1	Based on	WO 9930734

PRIORITY APPLN. INFO: US 1997-68080 19971218
AN 1999-395093 [33] WPIDS
AB WO 9930734 A UPAB: 19990819
NOVELTY - Venezuelan equine encephalitis (VEE) virus vectors can be used to express tumor-associated antigens and cytokines, and thus induce immunity to cancer.

DETAILED DESCRIPTION - A method of protecting or treating a subject against primary or metastatic neoplastic diseases, is new and comprises administering an effective amount of **recombinant** VEE virus vector (I) which comprises at least one attenuating mutation, and a heterologous DNA segment comprising a promoter operably-linked to a DNA encoding a protein or peptide effective for treating the disease. INDEPENDENT CLAIMS are also included for:

(1) a method of modulating tumours in a patient with (I);

(2) a method of inhibiting proliferation of tumor cells with (I);

(3) a process of inhibiting elevated levels of tumor cells, comprising administering to a host in need a therapeutically effective amount of (I) in unit dosage form;

(4) a process of treating primary or metastatic neoplastic diseases administering to a mammalian host in need a therapeutically

effective amount of (I) in unit dosage form, alternatively, a tumor-associated peptide is administered;

(5) a method of inhibiting the production of tumor cells in a patient comprising administering an effective amount of a tumor-associated peptide;

(6) a DNA comprising a cDNA clone coding for an infectious VEE virus RNA transcript and a heterologous promoter positioned upstream from the cDNA clone and operably associated therewith, further comprising at least one attenuating mutation and containing the nucleotide sequence encoding a TAA, a TAA peptide, or a natural or synthetic cytokine operably linked to a promoter;

(7) an infectious VEE RNA transcript encoded by the cDNA of (6);

(8) a method of treating a subject against primary or metastatic neoplastic diseases by infecting a subjects **dendritic** cells with a the transcript of (7);

(9) an inoculum comprising an effective amount of nucleic acid encoding the protein encoded by the cDNA of (6) dissolved or dispersed in an aqueous physiologically tolerable or pharmaceutically-acceptable diluent;

(10) a pharmaceutical composition comprising a therapeutically effective amount of (I) in a mixture with a pharmaceutically acceptable carrier, optionally further comprising an adjunctive agent selected from chemotherapeutic or immunotherapeutic agents.

USE - The VEE virus vectors of the invention can be used prevent, treat, and protect against primary and metastatic neoplastic diseases, especially tumors such as lung cancer, breast cancer, ovarian cancer, prostate cancer, pancreatic cancer, gastric cancer, colon cancer, renal cancer, bladder cancer, melanoma, hepatoma, sarcoma and lymphoma (all claimed).

ADVANTAGE - Cancer is a leading cause of death. Conventional cancer treatments consist of chemotherapy, radiotherapy and surgery. The VEE virus vectors of the invention circumvents these conventional therapies, and instead uses the natural defense system of the body against the cancer cell.

Dwg.0/0

L11 ANSWER 20 OF 33 MEDLINE DUPLICATE 5
ACCESSION NUMBER: 1999289594 MEDLINE
DOCUMENT NUMBER: 99289594 PubMed ID: 10359835
TITLE: **Recombinant Semliki Forest** virus and **Sindbis** virus efficiently infect neurons in hippocampal slice cultures.
AUTHOR: Ehrengruber M U; Lundstrom K; Schweitzer C; Heuss C; Schlesinger S; Gahwiler B H
CORPORATE SOURCE: Brain Research Institute, University of Zurich, Winterthurerstrasse 190, CH-8057 Zurich,

Switzerland.. ehrengru@hifo.unizh.ch
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1999 Jun 8) 96 (12) 7041-6.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990715
Last Updated on STN: 19990715
Entered Medline: 19990708

AB Gene transfer into nervous tissue is a powerful tool for the analysis of gene function. By using a rat hippocampal slice culture preparation, we show here that **Semliki Forest** virus (SFV) and **Sindbis** virus (SIN) vectors are useful for the effective infection of neurons. The stratum pyramidale and/or the granular cell layer were injected with **recombinant** virus encoding beta-galactosidase (LacZ) or green fluorescent protein (GFP). By using low concentrations of injected SFV-LacZ or SIN-LacZ, we detected LacZ staining of pyramidal cells, interneurons, and granule cells. About 60% of the infected cells showed clear neuronal morphology; thus, relatively few glial cells expressed the transgene. Expression of GFP from SFV and SIN vectors gave similar results, with an even higher percentage (>90%) of the GFP-positive cells identified as neurons. Infected pyramidal cells were readily recognized in living slices, displaying GFP fluorescence in **dendrites** of up to fourth order and in **dendritic** spines. They appeared morphologically normal and viable at 1-5 days postinfection. We conclude that both SFV and SIN vectors efficiently transfer genes into neurons in hippocampal slice cultures. In combination with the GFP reporter, SFV and SIN vectors will allow the physiological examination of identified neurons that have been modified by overexpression or suppression of a specific gene product.

L11 ANSWER 21 OF 33 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1999:767135 SCISEARCH
THE GENUINE ARTICLE: 242TE
TITLE: Induction of P815 tumor immunity by **recombinant Semliki Forest** virus expressing the P1A gene
AUTHOR: Colmenero P; Liljestrom P; Jondal M (Reprint)
CORPORATE SOURCE: KAROLINSKA INST, MICROBIOL & TUMORBIOL CTR, BOX 280, S-17177 STOCKHOLM, SWEDEN (Reprint); KAROLINSKA INST, MICROBIOL & TUMORBIOL CTR, S-17177 STOCKHOLM, SWEDEN; SWEDISH INST INFECT DIS CONTROL, DEPT

VACCINE RES, SOLNA, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: GENE THERAPY, (OCT 1999) Vol. 6, No. 10, pp. 1728-1733.
Publisher: STOCKTON PRESS, HOUNDMILLS, BASINGSTOKE RG21 6XS, HAMPSHIRE, ENGLAND.
ISSN: 0969-7128.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 54
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The methylcholantrene-induced P815 mastocytoma tumor is derived from DBA/2 mice and expresses a weak tumor rejection antigen, P815A. The PIA gene, which encodes for the P815A antigen, is silent in most normal tissues with the exception of testis and placenta. These characteristics make P815 an interesting mouse model for the human MAGE-type tumor antigens. **Recombinant Semliki Forest** virus particles (rSFV) were constructed that expressed variants of the P815 antigen. Such particles, when used for vaccination, express the antigen only transiently since the viral vector is incapable of productive replication. Nevertheless, mice vaccinated with rSFV generated strong CTL responses and were protected against P815 tumor challenge.

L11 ANSWER 22 OF 33 MEDLINE
ACCESSION NUMBER: 1999321252 MEDLINE
DOCUMENT NUMBER: 99321252 PubMed ID: 10395329
TITLE: Cancer therapy using a self-replicating RNA vaccine.
AUTHOR: Ying H; Zaks T Z; Wang R F; Irvine K R; Kammula U S; Marincola F M; Leitner W W; Restifo N P
CORPORATE SOURCE: Surgery Branch, National Cancer Institute, Bethesda, Maryland 20892-1502, USA.
SOURCE: NATURE MEDICINE, (1999 Jul) 5 (7) 823-7.
Journal code: CG5; 9502015. ISSN: 1078-8956.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199907
ENTRY DATE: Entered STN: 19990806
Last Updated on STN: 19990806
Entered Medline: 19990729

AB 'Naked' nucleic acid vaccines are potentially useful candidates for the treatment of patients with cancer, but their clinical efficacy has yet to be demonstrated. We sought to enhance the immunogenicity of a nucleic acid vaccine by making it 'self-replicating'. We accomplished this by using a gene encoding an RNA replicase

polyprotein derived from the **Semliki forest** virus, in combination with a model antigen. A single intramuscular injection of a self-replicating RNA immunogen elicited antigen-specific antibody and CD8+ T-cell responses at doses as low as 0.1 microg. Pre-immunization with a self-replicating RNA vector protected mice from tumor challenge, and therapeutic immunization prolonged the survival of mice with established tumors. The self-replicating RNA vectors did not mediate the production of substantially more model antigen than a conventional DNA vaccine did in vitro. However, the enhanced efficacy in vivo correlated with a caspase-dependent apoptotic death in transfected cells. This death facilitated the uptake of apoptotic cells by **dendritic** cells, providing a potential mechanism for enhanced immunogenicity. Naked, non-infectious, self-replicating RNA may be an excellent candidate for the development of new cancer vaccines.

L11 ANSWER 23 OF 33 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 6

ACCESSION NUMBER: 1999400725 EMBASE
TITLE: DNA and RNA-based vaccines: Principles, progress and prospects.
AUTHOR: Leitner W.W.; Ying H.; Restifo N.P.
CORPORATE SOURCE: N.P. Restifo, National Cancer Institute, National Institutes of Health, Building 10, Bethesda, MD 20892-1502, United States. restifo@nih.gov
SOURCE: Vaccine, (1999) 18/9-10 (765-777).
Refs: 142
ISSN: 0264-410X CODEN: VACCDE
PUBLISHER IDENT.: S 0264-410X(99)00271-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 022 Human Genetics
026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB DNA vaccines were introduced less than a decade ago but have already been applied to a wide range of infectious and malignant diseases. Here we review the current understanding of the mechanisms underlying the activities of these new vaccines. We focus on recent strategies designed to enhance their function including the use of immunostimulatory (CpG) sequences, **dendritic** cells (**DC**), co-stimulatory molecules and cytokine- and chemokine-adjuvants. Although genetic vaccines have been significantly improved, they may not be sufficiently immunogenic for

the therapeutic vaccination of patients with infectious diseases or cancer in clinical trials. One promising approach aimed at dramatically increasing the immunogenicity of genetic vaccines involves making them 'self-replicating'. This can be accomplished by using a gene encoding RNA replicase, a polyprotein derived from **alphaviruses**, such as **Sindbis** virus.
Replicase-containing RNA vectors are significantly more immunogenic than conventional plasmids, immunizing mice at doses as low as 0.1 .mu.g of nucleic acid injected once intramuscularly. Cells transfected with 'self-replicating' vectors briefly produce large amounts of antigen before undergoing apoptotic death. This death is a likely result of requisite double-stranded (ds) RNA intermediates, which also have been shown to super-activate **DC**. Thus, the enhanced immunogenicity of 'self-replicating' genetic vaccines may be a result of the production of pro-inflammatory dsRNA, which mimics an RNA-virus infection of host cells.

L11 ANSWER 24 OF 33 SCISEARCH
ACCESSION NUMBER: 1998:240119 SCISEARCH
THE GENUINE ARTICLE: ZC506
TITLE: Specific interactions between retrovirus Env and Gag proteins in rat neurons
AUTHOR: Weclewicz K; Ekstrom M; Kristensson K; Garoff H (Reprint)
CORPORATE SOURCE: KAROLINSKA INST, NOVUM, DEPT BIOSCI, S-14157 HUDDINGE, SWEDEN (Reprint); KAROLINSKA INST, NOVUM, DEPT BIOSCI, S-14157 HUDDINGE, SWEDEN; KAROLINSKA INST, DEPT NEUROSCI, S-17177 STOCKHOLM, SWEDEN
COUNTRY OF AUTHOR: SWEDEN
SOURCE: JOURNAL OF VIROLOGY, (APR 1998) Vol. 72, No. 4, pp. 2832-2845.
Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171.
ISSN: 0022-538X.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 38
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB In this work we have studied the intracellular Localization properties of the Gag and Env proteins of Moloney murine leukemia virus (MLV) and human immunodeficiency virus (HIV) in dorsal root ganglion (DRG) neurons of rat, These neurons form thick bundles of axons, which facilitates protein localization studies by immunofluorescence analyses. When such neuron cultures were infected with **recombinant Semliki Forest** virus
particles carrying the gag genes of either retrovirus, the expressed

Gag proteins were localized to both tile somatic and the axonal regions of the DRG neurons. In contrast, the Env proteins were confined only to the somatic region, When the Gag and Env proteins were coexpressed, the Gag proteins were also excluded from the axons. This effect of the Env proteins was shown to be dependent on the concentration of the Gag proteins in the neuron and also to be specific for homologous pairs of retrovirus proteins, Therefore, the results suggest that there are specific interactions between the Env and the Gag proteins of MLV and HIV in the DRG neurons.

L11 ANSWER 25 OF 33 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 1998:794689 SCISEARCH
THE GENUINE ARTICLE: 126TN
TITLE: Transfection of murine and human **dendritic** cells with **recombinant Semliki Forest** virus
AUTHOR: Bungener L (Reprint); Schoemaker M; Wilschut J; Daemen T
CORPORATE SOURCE: UNIV GRONINGEN, DEPT PHYSIOL CHEM, GROINGEN UTRECHT INST FRUG EXPLORAT, GRONINGEN, NETHERLANDS
COUNTRY OF AUTHOR: NETHERLANDS
SOURCE: JOURNAL OF LEUKOCYTE BIOLOGY, (OCT 1998) Supp. [2], pp. K2-K2.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0741-5400.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 0

L11 ANSWER 26 OF 33 SCISEARCH COPYRIGHT 2001 ISI (R)
ACCESSION NUMBER: 97:879389 SCISEARCH
THE GENUINE ARTICLE: YG424
TITLE: Transduction of human **dendritic** cells with **recombinant Semliki forest** virus coding for the ovarian carcinoma associated antigen alpha folate receptor for the generation of cytotoxic T cells from cancer patients.
AUTHOR: Albrecht B (Reprint); Kohler G; Mertelsmann R; Fisch P
CORPORATE SOURCE: UNIV FREIBURG, MED CTR, DEPT HEMATOL ONCOL, DEPT PATHOL, D-7800 FREIBURG, GERMANY; UNIV TUBINGEN, DIV IMMUNOL, TUBINGEN, GERMANY
COUNTRY OF AUTHOR: GERMANY
SOURCE: BLOOD, (15 NOV 1997) Vol. 90, No. 10, Part 1, Supp. [1], pp. 2454-2454.
Publisher: W B SAUNDERS CO, INDEPENDENCE SQUARE WEST

QP95768

CURTIS CENTER, STE 300, PHILADELPHIA, PA 19106-3399.
ISSN: 0006-4971.
DOCUMENT TYPE: Conference; Journal
FILE SEGMENT: LIFE; CLIN
LANGUAGE: English
REFERENCE COUNT: 0

L11 ANSWER 27 OF 33 BIOSIS COPYRIGHT 2001 BIOSIS
ACCESSION NUMBER: 1998:68763 BIOSIS
DOCUMENT NUMBER: PREV199800068763
TITLE: Transduction of human **dendritic** cells with **recombinant semliki forest** virus coding for the ovarian carcinoma associated antigen alpha folate receptor for the generation of cytotoxic T cells from cancer patients.
AUTHOR(S): Albrecht, B. (1); Koehler, G.; Mertelsmann, R.; Fisch, P.
CORPORATE SOURCE: (1) Univ. Freiburg Med. Cent., Dep. Hematol./Oncol., Freiburg Germany
SOURCE: Blood, (Nov. 15, 1997) Vol. 90, No. 10 SUPPL. 1 PART 1, pp. 551A.
Meeting Info.: 39th Annual Meeting of the American Society of Hematology San Diego, California, USA December 5-9, 1997 The American Society of Hematology . ISSN: 0006-4971.
DOCUMENT TYPE: Conference
LANGUAGE: English

L11 ANSWER 28 OF 33 MEDLINE DUPLICATE 7
ACCESSION NUMBER: 96392394 MEDLINE
DOCUMENT NUMBER: 96392394 PubMed ID: 8799182
TITLE: Expression and analysis of presenilin 1 in a human neuronal system: localization in cell bodies and **dendrites**.
AUTHOR: Cook D G; Sung J C; Golde T E; Felsenstein K M; Wojczyk B S; Tanzi R E; Trojanowski J Q; Lee V M; Doms R W
CORPORATE SOURCE: Department of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia 19104, USA.
CONTRACT NUMBER: P01 AG 11542 (NIA)
SOURCE: PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1996 Aug 20) 93 (17) 9223-8.
Journal code: PV3; 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961219
Last Updated on STN: 19980206
Entered Medline: 19961031

AB Mutations in the recently identified presenilin 1 gene on chromosome 14 cause early onset familial Alzheimer disease (FAD). Herein we describe the expression and analysis of the protein coded by presenilin 1 (PS1) in NT2N neurons, a human neuronal model system. PS1 was expressed using **recombinant Semliki Forest** virions and detected by introduced antigenic tags or antisera to PS1-derived peptides. Immunoprecipitation revealed two major PS1 bands of approximately 43 and 50 kDa, neither of which were N-glycosylated or O-glycosylated. Immunoreactive PS1 was detected in cell bodies and **dendrites** of NT2N neurons but not in axons or on the cell surface. PS1 was also detected in BHK cells, where it was also intracellular and colocalized with calnexin, a marker for the rough endoplasmic reticulum. A mutant form of PS1 linked to FAD did not differ from the wild-type protein at the light microscopic level. The model system described here will enable studies of the function of PS1 in human neurons and the role of mutant PS1 in FAD.

L11 ANSWER 29 OF 33 MEDLINE
ACCESSION NUMBER: 97050828 MEDLINE
DOCUMENT NUMBER: 97050828 PubMed ID: 8895567
TITLE: The beta-amyloid domain is essential for axonal sorting of amyloid precursor protein.
AUTHOR: Tienari P J; De Strooper B; Ikonen E; Simons M; Weidemann A; Czech C; Hartmann T; Ida N; Multhaup G; Masters C L; Van Leuven F; Beyreuther K; Dotti C G
CORPORATE SOURCE: Cell Biology Programme, European Molecular Biology Laboratories (EMBL), Heidelberg, Germany.
SOURCE: EMBO JOURNAL, (1996 Oct 1) 15 (19) 5218-29.
Journal code: EMB; 8208664. ISSN: 0261-4189.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199612
ENTRY DATE: Entered STN: 19970128
Last Updated on STN: 19980206
Entered Medline: 19961216

AB We have analysed the axonal sorting signals of amyloid precursor protein (APP). Wild-type and mutant versions of human APP were expressed in hippocampal neurons using the **Semliki forest** virus system. We show that wild-type APP and mutations implicated in Alzheimer's disease and another brain beta-amyloidosis are sorted to the axon. By analysis of deletion

mutants we found that the membrane-inserted APP ectodomain but not the cytoplasmic tail is required for axonal sorting. Systematic deletions of the APP ectodomain identified two regions required for axonal delivery: one encoded by exons 11-15 in the carbohydrate domain, the other encoded by exons 16-17 in the juxtamembraneous beta-amyloid domain. Treatment of the cells with the N-glycosylation inhibitor tunicamycin induced missorting of wild-type APP, supporting the importance of glycosylation in axonal sorting of APP. The data revealed a hierarchy of sorting signals on APP: the beta-amyloid-dependent membrane proximal signal was the major contributor to axonal sorting, while N-glycosylation had a weaker effect. Furthermore, recessive somatodendritic signals, most likely in the cytoplasmic tail, directed the protein to the **dendrites** when the ectodomain was deleted. Analysis of detergent solubility of APP and another axonally delivered protein, hemagglutinin, demonstrated that only hemagglutinin formed CHAPS-insoluble complexes, suggesting distinct mechanisms of axonal sorting for these two proteins. This study is the first delineation of sorting requirements of an axonally targeted protein in polarized neurons and indicates that the beta-amyloid domain plays a major role in axonal delivery of APP.

L11 ANSWER 30 OF 33 MEDLINE
ACCESSION NUMBER: 96032273 MEDLINE
DOCUMENT NUMBER: 96032273 PubMed ID: 7559765
TITLE: Intracellular routing of wild-type and mutated polymeric immunoglobulin receptor in hippocampal neurons in culture.
AUTHOR: de Hoop M; von Poser C; Lange C; Ikonen E; Hunziker W; Dotti C G
CORPORATE SOURCE: European Molecular Biology Laboratory, Cell Biology Program, Heidelberg, Germany.
SOURCE: JOURNAL OF CELL BIOLOGY, (1995 Sep) 130 (6) 1447-59. Journal code: HMV; 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199511
ENTRY DATE: Entered STN: 19951227
Last Updated on STN: 19970203
Entered Medline: 19951106

AB Certain epithelial cells synthesize the polymeric immunoglobulin receptor (pIgR) to transport immunoglobulins (Igs) A and M into external secretions. In polarized epithelia, newly synthesized receptor is first delivered to the basolateral plasma membrane and is then, after binding the Ig, transcytosed to the apical plasma membrane, where the receptor-ligand complex is released by

proteolytic cleavage. In a previous work (Ikonen et al., 1993), we implied the existence of a dendro-axonal transcytotic pathway for the rabbit pIgR expressed in hippocampal neurons via the **Semliki Forest** Virus (SFV) expression system. By labeling surface-exposed pIgR in live neuronal cells, we now show (a) internalization of the receptor from the **dendritic** plasma membrane to the **dendritic** early endosomes, (b) redistribution of the receptor from the **dendritic** to the axonal domain, (c) inhibition of this movement by brefeldin A (BFA) and (d) stimulation by the activation of protein kinase C (PKC) via phorbol myristate acetate (PMA). In addition, we show that a mutant form of the receptor lacking the epithelial basolateral sorting signal is directly delivered to the axonal domain of hippocampal neurons. Although this mutant is internalized into early endosomes, no transcytosis to the **dendrites** could be observed. In epithelial Madin-Darby Canine Kidney (MDCK) cells, the mutant receptor could also be internalized into basolaterally derived early endosomes. These results suggest the existence of a dendro-axonal transcytotic pathway in neuronal cells which shares similarities with the basolateral to apical transcytosis in epithelial cells and constitute the basis for the future analysis of its physiological role.

L11 ANSWER 31 OF 33 MEDLINE DUPLICATE 8
ACCESSION NUMBER: 93367860 MEDLINE
DOCUMENT NUMBER: 93367860 PubMed ID: 8360951
TITLE: Expression of heterologous proteins in cultured rat hippocampal neurons using the **Semliki Forest** virus vector.
AUTHOR: Olkkonen V M; Liljestrom P; Garoff H; Simons K; Dotti C G
CORPORATE SOURCE: Cell Biology Programme, European Molecular Biology Laboratory, Heidelberg, Germany.
SOURCE: JOURNAL OF NEUROSCIENCE RESEARCH, (1993 Jul 1) 35 (4) 445-51.
Journal code: KAC; 7600111. ISSN: 0360-4012.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199309
ENTRY DATE: Entered STN: 19931015
Last Updated on STN: 20000303
Entered Medline: 19930930

AB The **Semliki Forest** virus expression vector (Liljestrom and Garoff: Bio/Technology 9:1356-1361, 1991) was tested in cultured rat hippocampal neurons using two Madin-Darby canine kidney (MDCK) cell membrane-associated proteins as reporters: rab8,

a small GTPase involved in post-Golgi vesicle transport, and VIP21, an integral membrane protein of caveolae, trans-Golgi network, and post-Golgi vesicles. Expression of the c-myc epitope-tagged proteins was visualized by immunofluorescence microscopy. The proteins were first detected in neurons after 3-4 hr infection by the **recombinant** viruses. The infection efficiency on neurons was high: after 6 hr infection at a multiplicity of one, 50-60% of the cells expressed the reporter proteins. The neurons tolerated the infection well up to 8 hr. Their polarized organization was not disturbed, as judged from morphology and from distribution of the **dendritic** MAP2 and axonal synaptophysin marker proteins. The **Semliki Forest** virus vector thus seems suitable for short-term expression of proteins in cultured neurons.

L11 ANSWER 32 OF 33 MEDLINE DUPLICATE 9
ACCESSION NUMBER: 94012966 MEDLINE
DOCUMENT NUMBER: 94012966 PubMed ID: 8408204
TITLE: Protein transport to the **dendritic** plasma membrane of cultured neurons is regulated by rab8p.
AUTHOR: Huber L A; de Hoop M J; Dupree P; Zerial M; Simons K; Dotti C
CORPORATE SOURCE: Cell Biology Programme, European Molecular Biology Laboratory, Heidelberg, Germany.
SOURCE: JOURNAL OF CELL BIOLOGY, (1993 Oct) 123 (1) 47-55. Journal code: HMV; 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199311
ENTRY DATE: Entered STN: 19940117
Last Updated on STN: 20000303
Entered Medline: 19931102

AB In the companion paper (Huber, L. A., S. W. Pimplikar, R. G. Parton, H. Virta, M. Zerial, and K. Simons. J. Cell Biol. 123:35-45) we reported that the small GTPase rab8p is involved in transport from the TGN to the basolateral plasma membrane in epithelia. In the present work we investigated the localization and function of rab8p in polarized hippocampal neurons. By immunofluorescence microscopy we found that rab8p localized preferentially in the somatodendritic domain, and was excluded from the axon. Double-labeling immunofluorescence showed that some of the rab8p co-localized in the **dendrites** with the **Semliki Forest** Virus glycoprotein **E2** (SFV-**E2**). An antisense oligonucleotide approach was used to investigate the role of rab8p in **dendritic** transport of newly synthesized viral glycoproteins. Antisense oligonucleotides corresponding to the initiation region of the rab8 coding sequence were added to the

cultured neurons for four days. This treatment resulted in a significant decrease in cellular levels of rab8p and transport of SFV-**E2** from the cell body to the **dendrites** was significantly reduced. However, no effect was observed on axonal transport of influenza HA. From these results we conclude that rab8p is involved in transport of proteins to the **dendritic** surface in neurons.

L11 ANSWER 33 OF 33 CONFSCI COPYRIGHT 2001 CSA
ACCESSION NUMBER: 1998:26500 CONFSCI
DOCUMENT NUMBER: 98-026500
TITLE: Transduction of human **dendritic** cells with **recombinant Semliki Forest** virus coding for the ovarian carcinoma-associated antigen [alpha] folate receptor for the generation of cytotoxic T cells from cancer patients
AUTHOR: Albrecht, B.; Koehler, G.; Mertelsmann, R.; Fisch, P.
SOURCE: American Society for Hematology, 1200 19th Street, NW, Washington, DC 20036-2422; phone: 202-857-1118; fax: 202-857-1164; URL: http://www.hematology.org/, Abstracts available. Price $40. Poster Paper No. 2454

Meeting Info.: 974 0032: 39th Annual Meeting of the American Society for Hematology (9740032). San Diego, CA (USA). 5-9 Dec 1997. American Society for Hematology.
DOCUMENT TYPE: Conference
FILE SEGMENT: DCCP
LANGUAGE: English

FILE 'CAPLUS' ENTERED AT 11:47:36 ON 19 SEP 2001
L12 658 S SFV(S)SEMLIKI OR SIN(S)SINDBIS OR VEE(S)VENEZUEL?
L13 17 S RRV(S)ROSS
L14 12 S (L12 OR L13) AND (DENDRIT? OR DC(S)DENDRIT?)
L15 0 S L14 NOT L6

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, CONFSCI, SCISEARCH, JICST-EPLUS, JAPIO' ENTERED AT 11:50:14 ON 19 SEP 2001)
L16 42 S L14
L17 23 S L16 NOT L10
L18 0 S L17 AND ("E2" OR RESIDUE(5A)160 OR RECOMBINAN?)

=> fil hom
FILE 'HOME' ENTERED AT 11:51:18 ON 19 SEP 2001